Express Mail No.: ED 608 969 335 US

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| | ATTY. DOCKET NO. | APPLICATION NO. |
|---------------------------------------|------------------|-----------------|
| | 10165-037-999 | 10/520,140 |
| LIST OF REFERENCES CITED BY APPLICANT | APPLICANT | |
| (Use several sheets if necessary) | Brines et al. | |
| (Use several sheets if necessary) | FILING DATE | ART UNIT |
| | January 3, 2005 | 1647 |

| | | FOREIGN PATENT DOCUMENT COUNTRY CODE, NUMBER, KIND CODE (IF KNOWN) | DATE | NAME | PAGES, COLUMNS, LINES, WHERE RELEVANT PASSAGES OR RELEVANT FIGURES APPEAR | |
|---|------|--|----------|---|---|-------|
| /CMW/ | B01 | JP 5-246885 | 09/24/93 | JP-A Kokai | RELEVANT FIGURES AFFEAR | |
| /CMW/ | B02 | WO 94/24160 | 10/27/94 | Brigham and Women's Hospital | | |
| /CMW/ | B03 | WO 95/05465 | 02/23/95 | Amgen, Inc. | | |
| 000000000000000000000000000000000000000 | B04 | WO 97/18318 | 05/22/97 | Takara Shuza CoLtd | 000000000000000000000000000000000000000 | 00000 |
| /CMW/ | B05 | WO 97/32895 | 12/12/97 | Regents of the University of California | | |
| /CMW/ | B06 | WO 98/18926 | 05/07/98 | G.D. Searle & Co. | | |
| 000000000000000000000000000000000000000 | -B07 | WO.00/35475 | 06/22/00 | Ehrenreich | 300000000000000000000000000000000000000 | 20000 |
| /CMW/ | B08 | WO 01/82952 | 11/08/01 | Action Pharma APS | | |
| 8 | B09 | WO 01/82953 | 11/08/01 | Action Pharma APS | | |
| | B10 | EP 555880 | 08/18/93 | Bristol-Myers Squibb Company | | |
| 1, | B11 | WO 92/08493 | 5/29/92 | Brigham & Women's Hospital | | _ |
| $\overline{}$ | B12 | WO 96/14081 | 5/17/96 | Boehringer Manheim gmbh | | |
| /CMW/ | B13 | WO 02/10743 | 2/07/02 | Ortho-McNeil Pharmaceutical, Inc. | | _ |

| | | NON PATENT LITERATURE DOCUMENTS | |
|----------------------|-----|---|---|
| Examiner Initials |] | (Include name of the author (in CAPITAL LETTERS), Title, Date, Pertinent Pages, Etc.) | |
| /CMW/ | C01 | ALAFACI et al., 2000, "Effect of Recombinant Human Erythropoietin on Cerebral Ischemia Following Experimental Subarachnoid Hemorrhage," Eur. J. Phar., 406:219-225. | 1 |
| 1000000000 | C02 | ANAGNOSTOU et al., 1994, "Erythropoietin receptor mRNA expression in human endothelial cells", Proc. Natl. Acad. Sci. USA 91:3974-3978 | |
| 900000000 | C03 | ANNABLE et al., 1972, "The Second International Reference Preparation of Erythropoietin, Human, Urinary, for Bioassay," Bull. Org. mond. Sante, 47:99-112. | |
| 000000000 | C04 | ASHWELL et al., 1978, "A Protein from Mammalian Liver that Specifically Binds Galactose-Terminated Glycoproteins," Meth. Enzymol., 50:287-291. | |
| 000000000 | C05 | BAUER, 1995, "The Oxygen Sensor That Controls EPO Production: Facts and Fancies," J. Perinat. Med., 23:7-12. | |
| 20000000 | C06 | BENYO et al., 1999, "Expression of erythropoietin receptor by trophoblast cells in the human placenta", Biol. Reproduct. 60:861-870 | |
| 000000 | C07 | BERNAUDIN et al., 1999, "A potential role for erythropoietin in focal permanent cerebral ischemia in mice", J. Cereb. Blood Flow Metab. 19:643-651 | |
| V | C08 | BERNAUDIN et al., 2000, "Neurons and astrocytes express EPO mRNA: oxygen-sensing mechanisms that involve the redox-state of the brain", Glia 30:271-278 | |
| /CMW/ | C09 | BONDY, 1995, "The relaxation of oxidative stress and hyperexcitation to neurological disease", Proc. Soc. Exp. Biol. Med. 208:337-345 | |

| | EXAMINER NYI-3972311v2 | /Cherie M. Woodward/ | DATE CONSIDERED | 12/21/2007 |
|--|---------------------------|----------------------|-----------------|------------|
|--|---------------------------|----------------------|-----------------|------------|

^{*}EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Express Mail No.: *ED 608 969 335 US*

Sheet 3 of 7 of List of References

| | ATTY. DOCKET NO. | APPLICATION NO. |
|---------------------------------------|------------------|-----------------|
| | 10165-037-999 | 10/520,140 |
| LIST OF REFERENCES CITED BY APPLICANT | APPLICANT | |
| (Use several sheets if necessary) | Brines et al. | |
| | FILING DATE | ART UNIT |
| | January 3, 2005 | 1647 |

| | , | NON PATENT LITERATURE DOCUMENTS | |
|------------------|----------|---|---------|
| Examiner | | (Include none of the outhor (in CADITAL LETTERS) Title Date Berlin at Barry Etc.) | T |
| nitials /CMW/ | | (Include name of the author (in CAPITAL LETTERS), Title, Date, Pertinent Pages, Etc.) BRIGGS et al., 1974, "Hepatic Clearance of Intact and Desialylated Erythropoietin," Am. J. Physiol., 227:1385- | +' |
| / CIVI V V / | C10 | 1388. | |
| | C11 | BRINES et al., 2000, "Erythropoietin crosses the blood-brain barrier to protect against experimental brain | t |
| | | injury", Proc. Natl. Acad. Sci. USA 97:10526-10531 | 1 |
| | C12 | BRUNEVAL et al., 1993, "Erythropoietin Synthesis by Tumor Cells in a Case of Meningioma Associated With | T |
| | <u> </u> | Erythrocytosis," Blood, 81:1593-1597. | ┖ |
| | C13 | CAMISCOLI et al., 1968, "Comparative Assay of Erythropoietin Standards," Annals New York Acad. Sci., | |
| | 1 | 149:40-45. | 1 |
| | C14 | CAMPANA et al., 1998, "Identification of a neurotrophic sequence in erythropoietin", Int. J. Mol. Med. 1:235-241 | |
| | C15 | CLAUS-WALKER et al., 1984, "Spinal Cord Injury and Serum Erythropoietin," Arch. Phys. Med. Rehabil., | ╀ |
| | C15 | 65:370-374. | |
| | C16 | COTES, 1968, "Quantitative Estimation of Erythropoietin," Part I. Assay and Standardization of | T |
| | 0.0 | Erythropoietin, Annals New York Acad. Sci., 149:12-17. | ١ |
| | C17 | COTES et al., 1961, "Bio-Assay of Erythropoietin in Mice Made Polycythaemic By Exposure to Air at a | T |
| | | Reduced Pressure," Nature, 191:1065-1067. | L |
| | C18 | COTES et al., 1966, "The International Reference Preparation of Erythropoietin," Bull. Org. mond. Sante, | ı |
| | ļ | 35:751-760. | 4- |
| | C19 | DIAZ-BRINTON et al., 1998, "Advances and challenges in the prevention and treatment of Alzheimer's disease," Pharm. Res. 15(3):386-98 | ı |
| | 620 | DIGICAYLIOGLU et al. 1995, "Localization of specific erythropoietin binding sites in defined areas of the | + |
| | C20 | mouse brain.", Proc. Natl. Acad. Sci. USA 92:3717-3720 | |
| | C21 | DIPAOLO et al., 1992, "Effects of uremia and dialysis on brain electrophysiology after recombinant | t |
| | 02. | erythropoietin treatment", ASAIO J. 38:M477-M480 | 1 |
| | C22 | DONG et al., 1992, "Receptor binding of asialoerythropoietin," J. Cell. Biochem. 48(3):269-76 | Τ |
| | C23 | DORDAL et al., 1985, "The Role of Carbohydrate in Erythropoietin Action," Endocrinol., 116:2293-2299. | t |
| | C24 | DUBE et al, 1988, "Glycosylation at Specific Sites of Erythropoietin is Essential for Biosynthesis, Secretion, | ╁ |
| | C24 | and Biological Function," J. Biol. Chem., 263:17516-17521. | 1 |
| | C25 | EHRENREICH et al., 2002, "Erythropoietin therapy for acute stroke is both safe and beneficial", Molec. Med. | T |
| | | 8(8):495-505 | L |
| | C26 | Eur. Pharmacopoeia, 1997, p. 5. | |
| | C27 | Eur. Pharmacopoeia, Suppl. 2001, pp. 777-782. | T |
| | C28 | FARRELL et al., 2001, "Erythropoietin crosses the blood brain barrier", Blood 98:148b (abstr. # 4265; 43rd | + |
| | 1 020 | Annual Meeting of the American Society of Hematology, Orlando FL, Dec. 7-11, 2001) | ı |
| | C29 | FEIGIN et al., 2002, "Recent advances in Huntington's disease: implications for experimental therapeutics," | Ť |
| | 1 | Curr. Opin. Neurol. 15(4):483-9 | L |
| 2000 | C30 | FUKUDA et al., 1989, "Survival of Recombinant Erythropoietin in the Circulation: The Role of | Γ |
| | ļ | Carbohydrates," Blood, 73:84-89. | 1 |
| | C31 | GARTHOFF, 1995, "Safety and Efficacy Testing of Hormones and Related Products," The Report and | 1 |
| V | | Recommendations of ECVAM Workshop 9, A.T.L.A., 23:699-711 | \perp |
| /ČMW/ | C32 | GOLDWASSER et al., 1974, "On the Mechanism of Erythropoietin-Induced Differentiation," XIII. The Role of Sialic Acid in Erythropoietin Action, J. Biol. Chem., 249:4202-4206. | |

| EXAMINER 1Y1-3972311v2 | /Cherie M. Woodward/ | DATE CONSIDERED | 12/21/2007 |
|-------------------------------|----------------------|-----------------|------------|
| | | | |

^{*}EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Express Mail No.: *ED 608 969 335 US*

Sheet 4 of 7 of List of References

| | ATTY. DOCKET NO. 10165-037-999 | APPLICATION NO. 10/520,140 |
|---|--------------------------------|----------------------------|
| LIST OF REFERENCES CITED BY APPLICANT (Use several sheets if necessary) | APPLICANT Brines et al. | |
| | FILING DATE January 3, 2005 | art unit 1647 |

| Examiner | T | | 1 |
|---|-----|--|-----------|
| nitials | | (Include name of the author (in CAPITAL LETTERS), Title, Date, Pertinent Pages, Etc.) | Т |
| /CMW/ | C33 | GOLDWASSER et al., 1975, "An Assay for Erythropoietin in Vitro at the Milliunit Level," Endo., 97:315-323. | |
| X000000 | C34 | GOLDWASSER et al., "Erythropoietin: Assay and Study of Its Mode of Action," Hormone Assays, pp. 109- | - |
| | C35 | GORIO et al., 2002, "Recombinant human erythropoietin counteracts secondary injury and markedly enhances neurological recovery from experimental spinal cord trauma", Proc. Natl. Acad. Sci. USA 99:9450-9455 (PNAS Early Edition www.pnas.org/cgi/doi/10.1073/pnas.142287899) | |
| 000000000000000000000000000000000000000 | C36 | GRASSO et al., 2002, "Beneficial effects of systemic administration of recombinant human erythrpoietin in rabbits subjected to subarachnoid hemorrhage", Proc. Natl. Acad. Sci. USA 99:5627-5631 | |
| 3000000 | C37 | GREGORY et al., 1999, "GATA-1 and erythropoietin cooperate to promote erythroid cell survival by regulating bcl-xL expression", Blood 94:87-96 | T |
| | C38 | GRIMM et al., 1990, "Improvement of brain function in hemodialysis patients treated with erythropoietin", Kidney Intl. 38:480-486 | |
| 0000 | C39 | HAMMOND et al., 1968, "Production, Utilization and Excretion of Erythropoietin: I. Chronic Anemias. II. Aplastic Crisis. III. Erythropoietic Effects of Normal Plasma," Erythropoietin, 149:516-527. | |
| 00000 | C40 | HEFTI, 1997, "Pharmacology of neurotrophic factors", Annu. Rev. Pharmacol. Toxicol. 37:239-267 | Γ |
| | C41 | HENGEMIHLE et al., 1996, "Chronic treatment with human recombinant erythropoietin increases hematocrit and improves water maze performance in mice", Physiol. Behav. 59:153-156 | |
| 00000000 | C42 | HIRAKATA et al., 1992, "CBF and oxygen metabolism in hemodialysis patients: effects of anemia correction with recombinant human EPO", Am. J. Physiol. 262:F737-F743 | Ī |
| 000000000000000000000000000000000000000 | C43 | HORTON et al., 1991, "Von Hippel-Lindau Disease and Erythrocytosis: Radioimmunoassay of Erythropoietin in Cyst Fluid From a Brainstem Hemangioblastoma," Neurology, 41:753-754. | T |
| 3333333333 | C44 | IMAI et al., 1990, "Physicochemical and Biological Characterization of Asialoerythropoietin," Eur. J. Biochem., 194:457-462. | |
| 0000000 | C45 | JOOSS et al., 1996, "Cyclophosphamide diminishes inflammation and prolongs transgene expression following delivery of adenoviral vectors to mouse liver and lung," Hum. Gene Ther. 7(13):1555-66 | |
| 000000000000000000000000000000000000000 | C46 | JUNK et al., 2002, "Erythropoietin administration protects retinal neurons from acute ischemia-reperfusion injury", Proc. Natl. Acad. Sci. USA 99:10659-10664 (PNAS Early Edition | |
| | C47 | www.pnas.org/cgi/doi/10.1073/pnas.152321399) JUUL et al., 1998, "Erythropoietin and erythropoietin receptor in the developing human central nervous system", Pediatr. Res. 43:40-49 | |
| ×××××××××××××××××××××××××××××××××××××× | C48 | JUUL et al., 1998, "Tissue distribution of erythropoietin and erythropoietin receptor in the developing human fetus", Early Human Devel. 52:235-249 | |
| 000000000000000000000000000000000000000 | C49 | JUUL et al., 2001, "Recombinant erythropoietin (EPO) crosses the blood brain barrier (BBB) in preterm fetal sheep", Soc. for Neuroscience Abstracts 27:929 (31st Annual Meeting of the Society for Neuroscience, San Diego, CA Nov. 10-15, 2001) | |
| 000000000000000000000000000000000000000 | C50 | KEIGHLEY, 1968, "Further Experiences with Assays, Units, and Standards of Erythropoietin," Annals New York Acad. Sci., 149:18-24. | |
| | C51 | KOHAMA et al., 2000, "Large Uterine Myoma with Erythropoietin Messenger RNA and Erythrocytosis," Obstetrics and Gynecology, 96:826-828. | T |
| V | C52 | KONISHI et al., 1993, "Trophic effect of erythropoietin and other hematopoietic factors on central cholinergic neurons in vitro and in vivo", Brain Res. 609:29-35 | |
| /CMW/ | C53 | KOPF et al., 1994, "Memory improving actions of glucose: involvement of a central cholinergic muscarinic | \dagger |

|--|

^{*}EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Express Mail No.: ED 608 969 335 US

Sheet 5 of 7 of List of References

| | ATTY. DOCKET NO. | APPLICATION NO. |
|---------------------------------------|------------------|-----------------|
| | 10165-037-999 | 10/520,140 |
| LIST OF REFERENCES CITED BY APPLICANT | APPLICANT | |
| (Use several sheets if necessary) | Brines et al. | |
| | FILING DATE | ART UNIT |
| | January 3, 2005 | 1647 |

| | | NON PATENT LITERATURE DOCUMENTS | |
|---|-----|--|---|
| Examiner Initials | | (Include name of the author (in CAPITAL LETTERS), Title, Date, Pertinent Pages, Etc.) | 7 |
| /CMW/ | C54 | LATINI et al., 1998, "Comparative efficacy of a DA2/α2 agonist and a β blocker in reducing adrenergic drive and cardiac fibrosis in an experimental model of left ventricular dysfunction after coronary artery occlusion", J. Cardiovasc. Pharmacol. 31:601-608 | |
| | C55 | LI et al., 1996, "Erythropoietin receptors are expressed in the central nervous system of mid-trimester human fetuses", Pediatr. Res. 40:376-380 | |
| 300000000000000000000000000000000000000 | C56 | LI et al., 1998, "A single pre training glucose injection induces memory facilitation in rodents performing various tasks: contribution of acidic fibroblast growth factor", Neurosci. 85:785-794 | |
| 00000000 | C57 | LIPINSKI et al., 1995, "Nerve growth factor facilitates conditioned taste aversion learning in normal rats", Brain Res. 692:143-153 | |
| 000000000 | C58 | LIU et al., 1996, "Transgenic mice containing the human erythropoietin receptor gene exhibit correct hematopoietic and neural expression", Proc. Assoc. Am. Physicians 108:449-454 | |
| 0000 | C59 | LIU et al., 1997, "Regulated human erythropoietin receptor expression in mouse brain", J. Biol. Chem. 272:32395-32400 | |
| 355555555 | C60 | LIU et al., 1994, "Tissue specific expression of human erythropoietin receptor in transgenic mice", Devel. Biol. 166:159-169 | |
| 3000000000 | C61 | LOWY et al., 1960, "Inactivation of Erythropoietin by Neuraminidase and by Mild Substitution Reactions," Nature, 185:102-103. | |
| 000000000000000000000000000000000000000 | C62 | MARRERO et al., 1998, "Erythropoietin receptor-operated Ca2+ channels: activation by phospholipase C-γ1", Kidney Intl. 53:1259-1268 | |
| 300000000 | C63 | MARSH et al., 1991, "rHuEPO treatment improves brain and cognitive function of anemic dialysis patients", Kidney Intl. 39:155-163 | Ī |
| 000000000000000000000000000000000000000 | C64 | MARTI et al., 1997, "Detection of erythropoietin in human liquor: intrinsic erythropoietin production in the brain", Kidney Intl. 51:416-418 | Ī |
| 000000000 | C65 | MARTI et al., 1996, "Erythropoietin gene expression in human, monkey and murine brain", Eur. J. Neurosci. 8:666-676 | Ī |
| 000000000000000000000000000000000000000 | C66 | MASUDA et al., 1997, "Insulin like growth factors and insulin stimulate erythropoietin production in primary cultured astrocytes", Brain Res. 746:63-70 | |
| 000000000000000000000000000000000000000 | C67 | MASUDA et al., 1994, "A novel site of erythropoietin production. Oxygen dependent production in cultured rat astrocytes", J. Biol. Chem. 269:19488-19493 | Ī |
| 000000000000000000000000000000000000000 | C68 | MASUDA et al., 1993, "Functional erythropoietin receptor of the cells with neural characteristics. Comparison with receptor properties of erythroid cells", J. Biol. Chem. 268:11208-11216 | T |
| 000000000000000000000000000000000000000 | C69 | MATSUYAMA et al., 2000, "Erythrocytosis Caused by an Erythropoietin-Producing Hepatocellular Carcinoma," J. Surg. Oncology, 75:197-202. | |
| 00000000 | C70 | MIONI et al., 1992, "Evidence for specific binding and stimulatory effects of recombinant human erythropoietin on isolated adult rat Leydig cells", Acta Endocrinologica 127:459-465 | |
| 2000000 | C71 | MIYAKE et al., 1977, "Purification of Human Erythropoietin," J. Biol. Chem., 252:5558-5564. | |
| V | C72 | MORELL et al., 1968, "Physical and Chemical Studies on Ceruloplasmin," Metabolic Studies on Sialic Acid- Free Ceruloplasmin In Vivo, J. Biol. Chem., 243:155-159. | T |
| 0000000000 | C73 | MORISHITA et al., 1997, "Erythropoietin receptor is expressed in rat hippocampal and cerebral cortical neurons, and erythropoietin prevents in vitro glutamate induced neuronal death", Neurosci. 76:105-116 | |
| V | C74 | MOSS et al., 1996, "Oxygen administration enhances memory formation in healthy young adults", Psychopharmacol. 124:255-260 | |
| /ČMW/ | C75 | NAKAMURA et al., 1998, "Elevated levels of erythropoietin in cerebrospinal fluid of depressed patients", Am. | T |

| EXAMINER NYI-3972311v2 | /Cherie M. Woodward/ | DATE CONSIDERED | 12/21/2007 |
|---------------------------|--|--|---|
| *EXAMINER: Initia | al if reference considered, whether or not citation is in conf | formance with MPFP 609: Draw line thro | ough citation if not in conformance and not |

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Express Mail No.: *ED 608 969 335 US*

Sheet 6 of 7 of List of References

| | ATTY. DOCKET NO. 10165-037-999 | APPLICATION NO. 10/520,140 |
|---|--------------------------------|----------------------------|
| LIST OF REFERENCES CITED BY APPLICANT (Use several sheets if necessary) | APPLICANT Brines et al. | |
| | FILING DATE January 3, 2005 | ART UNIT 1647 |

| | | NON PATENT LITERATURE DOCUMENTS | |
|---|-----|---|--------------|
| Examiner Initials /CMW/ | | (Include name of the author (in CAPITAL LETTERS), Title, Date, Pertinent Pages, Etc.) J. Med. Sci. 315:199-201 | Т |
| /CIVIVV/ | | | |
| 0000000 | C76 | NISSENSON et al., 1991, "Recombinant human erythropoietin and renal anemia: molecular biology, clinical efficacy and nervous system effects", Ann. Int. Med. 114:402-416 | |
| 000000 | C77 | NISSENSON, 1989, "Recombinant human erythropoietin: impact on brain and cognitive function, exercise tolerance, sexual potency and quality of life", Sem. Nephrol. 9(suppl. 2):25-31 | |
| XXXXXXXXXXX | C78 | OGDEN, 1989, "Monitoring considerations in recombinant human erythropoietin therapy", Sem. Nephrol. 9(suppl. 2):12-15 | |
| 000000000000000000000000000000000000000 | C79 | OKADA et al., 1996, "Erythropoietin stimulates proliferation of rat-cultured gastric mucosal cells", Digestion 57:328-332 | |
| 3000 | C80 | PARDRIDGE, 1997, "Drug delivery to the brain", J. Cerebral Blood Flow Metab. 17:713-731 | |
| 00000 | C81 | PARDRIDGE et al., 1991, "Selective transport of an anti-transferrin receptor antibody through the blood-brain barrier in vivo", J. Pharmacol. Exp. Ther. 27:66-70 | |
| | C82 | PLAPP et al., 1971, "Activity of bovine pancreatic deoxyribonuclease A with modified amino groups," J. Biol. Chem. 246(4):939-45 | |
| | C83 | PODUSLO et al., 1994, "Macromolecular premeability across the blood-nerve and blood-brain barriers", Proc. Natl. Acad. Sci. USA 91:5705-5709 | |
| | C84 | PRENDERGAST et al., 1997, "Nitric oxide synthase inhibition impairs spatial navigation learning and induces conditioned taste aversion", Pharmacol. Biochem. Behav. 57:347-352 | |
| | C85 | ROBINSON et al., 1975, "Tetanus toxin. The effect of chemical modifications on toxicity, immunogenicity, and conformation," J. Biol. Chem. 250(18):7435-42 | |
| 000000 | C86 | ROSE et al., 1998, "Receptor-mediated angiotensin II transcytosis by brain microvessel endothelial cells", Peptides 19:1023-1030 | |
| | C87 | SADAMATO et al., 1998, "Erythropoietin prevents place navigation disability and cortical infarction in rats with permanent occlusion of the middle cerebral artery", Biochem. Biophys. Res. Comm. 253:26-32 | |
| | C88 | SAKANAKA et al., 1998, "In vivo evidence that erythropoietin protects neurons from ischemic damage", Proc. Natl. Acad. Sci. USA 95:4635-4640 | 1 |
| | C89 | SATAKE et al. 1990, "Chemical modification of erythropoietin: an increase in in vitro activity by guanidination," Biochim. Biophys. Acta. 1038(1):125-9 | |
| 20000000 | C90 | SAWYER et al., 1989, "Receptors for erythropoietin in mouse and human erythroid cells and placenta", Blood 74:103-109 | T |
| 20000 | C91 | SHIRAMIZU et al., 1994, "Constitutive Secretion of Erythropoietin by Human Renal Adenocarcinoma Cells in Vivo and in Vitro," Exp. Cell Res., 215:249-256. | - |
| | C92 | SHORE et al., 1968, "Quantitative Estimation of Erythropoietin," Annals New York Acad. Sci., 149:46-48. | + |
| | C93 | SILVA et al., 1999, "Erythropoietin can induce the expression of bcl-xL through Stat5 in erythropoietin- dependent progenitor cell lines", J. Biol. Chem. 274:22165-22169 | |
| 999 | C94 | SIRÉN et al., 2001, "Erythropoietin prevents neuronal apoptosis after cerebral ischemia and metabolic stress", Proc. Natl. Acad. Sci. USA 98:4044-4049 | T |
| | C95 | SPIVAK et al., 1989, "The In Vivo Metabolism of Recombinant Human Erythropoietin in the Rat," Blood, 73:90-99. | T |
| V | C96 | STARK et al., 1960, "Reactions of the Cyanate Present in Aqueous Urea With Amino Acids and Proteins," J. | |
| ▼ | + | Biol. Chem. 235(11): 3177-3181 | + |
| /CMW/ | C97 | STEECE-COLLIER et al., 2002, "Etiology of Parkinson's disease: Genetics and environment revisited," Proc. | |

| EXAMINER NYI-3972311v2 | /Cherie M. Woodward/ | DATE CONSIDERED | 12/21/2007 |
|---------------------------|----------------------|-----------------|------------|
| 1 | | | |

^{*}EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Express Mail No.: <u>ED 608 969 335 US</u>

Sheet 7 of 7 of List of References

| | ATTY. DOCKET NO. 10165-037-999 | APPLICATION NO. 10/520,140 |
|---|--------------------------------|----------------------------|
| LIST OF REFERENCES CITED BY APPLICANT (Use several sheets if necessary) | APPLICANT Brines et al. | |
| | FILING DATE January 3, 2005 | ART UNIT |

| | | NON PATENT LITERATURE DOCUMENTS | |
|---|------|---|---|
| Examiner nitials | | (Include name of the author (in CAPITAL LETTERS), Title, Date, Pertinent Pages, Etc.) | Т |
| /CMW/ | | Natl. Acad. Sci. U. S. A. 99(22):13972-4 | |
| 000000 | C98 | STORRING et al., 1998, "Epoietin Alfa and Beta Differ In Erythropoietin Isoform Compositions and Biological Properties," British J. Haematology, 100:79-89. | |
| >====================================== | C99 | STORRING et al., 1992, "The International Standard for Recombinant DNA-Derived Erythropoietin: Collaborative Study of Four Recombinant DNA-derived Erythropoietins and Two Highly Purified Human Urinary Erythropoietins," J. Endocrinol., 134:459-484. | |
| 0000000000 | C100 | SUZUKI et al., 2001, "Erythropoietin Synthesis by Tumour Tissues in a Patient With Uterine Myoma and ERythrocytosis," British J. Haematology, 113:49-51. | |
| 000000000000000000000000000000000000000 | C101 | TABIRA et al., 1995, "Neurotrophic effect of hematopoietic cytokines on cholinergic and other neurons in vitro", Int. J. Devl. Neurosci. 13:241-252 | |
| 0000 | C102 | WEILAND et al., "In vivo Activity of Asialo-Erythropoietin in Combination with Asialo-Glycoproteins," 1982, Blut, 44:173-175. | |
| | C103 | WESTENFELDER et al., 1999, "Human, rat and mouse kidney cells express functional erythropoietin receptors", Kidney Intl. 55:808-820 | |
| | C104 | WILLIAMS et al., 1994, "Human erythropoietin receptor", Ann. NY Acad. Sci. 718:232-244 | T |
| | C105 | WOLCOTT et al., 1989, "Recombinant human erythropoietin treatment may improve quality of life and cognitive function in chronic hemodialysis patients", Am. J. Kidney Dis. 14:478-485 | |
| | C106 | WU et al., 1999, "Neuroprotection with noninvasive neurotrophin delivery to the brain", PNAS 96:254-259 | |
| V | C107 | YAMAJI et al., 1996, "Brain capillary endothelial cells express two forms of erythropoietin receptor mRNA", Eur. J. Biochem. 239:494-500 | |
| /CMW/ | C108 | YANG et al., 2002, "Effects of ammonia and glucosamine on the heterogeneity of erythropoietin glycoforms," Biotechnol. Prog. 18(1):129-38 | |

| EXAMINER /Cherie M. Woodward/ NYI-3972311v2 | DATE CONSIDERED 12/21/2007 |
|--|----------------------------|
|--|----------------------------|

^{*}EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

| SEP 2 8 2007 Filing date ART UNIT | LIST OF REFERENCES CITED BY APPLICANT (Use several sheets if necessary) | 10165-037-999 APPLICANT | APPLICATION NO. 10/520,140 (National Stage of PCT/US2003/021350) |
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| (SEP 2, 8 LOUI FILING DATE ART UNIT | 0 2007 180 | Brines et al. | |
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| | | | U.S. P. | ATENT DOCUMENTS | |
|----------|-----|-----------------|----------|------------------|---|
| EXAMINER | | DOCUMENT NUMBER | DATE | NAME | PAGES, COLUMNS, LINES, WHERE RELEVANT PASSAGES OR RELEVANT FIGURES APPEAR |
| /CMW/ | A01 | 4,377,513 | 03/22/83 | Sugimoto et al. | |
| | A02 | 4,703,008 | 10/27/87 | Lin | |
| | A03 | 4,806,524 | 02/21/89 | Kawaguchi et al. | |
| | A04 | 4,835,260 | 05/30/89 | Shoemaker | |
| | A05 | 5,457,089 | 10/10/95 | Fibi et al. | |
| | A06 | 5,547,933 | 08/20/96 | Lin | |
| 1 | A07 | 5,571,787 | 11/05/96 | O'Brien et al. | |
| | A08 | 5,614,184 | 03/25/97 | Sytkowski et al. | |
| | A09 | 5,618,698 | 04/08/97 | Lin | |
| 1 | A10 | 5,621,080 | 04/15/97 | Lin | |
| 1 | All | 5,625,035 | 04/29/97 | Clemons | |
| | A12 | 5,661,125 | 08/26/97 | Strickland | |
| | A13 | 5,696,080 | 12/09/97 | O' Brien | |
| | A14 | 5,700,909 | 12/23/97 | O'Brien | |
| | A15 | 5,714,459 | 02/03/98 | O'Brien | |
| | A16 | 5,756,349 | 05/26/98 | Lin | |
| | A17 | 5,767,078 | 06/16/98 | Johnson et al. | |
| | A18 | 5,773,569 | 06/30/98 | Wrighton et al. | |
| | A19 | 5,830,851 | 11/03/98 | Wrighton et al. | |
| | A20 | 5,835,382 | 11/10/98 | Wilson et al. | |
| | A21 | 5,856,298 | 01/05/99 | Strickland | |
| | A22 | 5,888,772 | 03/30/99 | Okasinski et al. | |
| | A23 | 5,955,422 | 09/21/99 | Lin | |
| V | A24 | 6,165,783 | 12/26/00 | Weiss et al. | |
| -KOMW/ | A25 | 4,658,019 | 04/14/87 | Kung et al. | |

FOREIGN PATENT DOCUMENTS

| EXAMINER NYI-3972311v2 /Cherie M. Woodward/ DATE CONSIDERED 12/21/2007 |
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^{*}EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

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| | ATTY. DOCKET NO. | APPLICATION NO. 10/520,140 |
| LIST OF REEDENICES CITED DV ADDLICANT | 10165-037-999 | (National Stage of PCT/US2003/021350) |
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| B01 | JP 5-246883 | 09/24/93 | JP-A Kokai | | |
| B02 | WO 94/24160 | 10/27/94 | Brigham and Women's Hospital | | |
| B03 | WO 95/05465 | 02/23/95 | Amgen, Inc. | | |
| B04 | WO 97/18318 | 05/22/97 | Takara Shuzo Co., Ltd. | | |
| B05 | WO 97/32895 | 12/12/97 | Regents of the University of California | - | |
| B06 | WO 98/18926 | 0 (07/98 | G.D. Searle & Co. | | |
| B07 | WO 00/35475 | 06/22/00 | Ehrenreich | | |
| B08 | WO 01/82952 | 11/08/01 | Action Pharma APS | | |
| B09 | WO 01/82953 | 11/08/01 | Action Pharma APS | | |
| B10 | EP 555880 | 08/18/93 | Bristol-Myers Squibb Company | | |
| B11 | WO 92/08493 | 5/29/92 | Brigham & Women's Hospital | | |
| B12 | WO 96/14081 | 5/17/96 | Boeringer Manheim gmbh | | |
| B13 | WO 02/10743 | 2/07/02 | Orth-McNeil Pharmaceutical, Inc. | | |
| | | | | | |

| NON PATENT LITERATURE DOCUMENTS | | | |
|---------------------------------|-----|---|----------|
| Examiner Initials | | (Include name of the author (in CAPITAL LETTERS), Title, Date, Pertinent Pages, Etc.) | Т |
| milais | C01 | ALAFACI et al., 2000, "Effect of Recombinant Human Eryth opoietin on Cerebral Ischemia Following Experimental Subarachnoid Hemorrhage," Eur. J. Phar., 406:219-225. | <u> </u> |
| - | C02 | ANAGNOSTOU et al., 1994, "Erythropoietin receptor mRNA expression in human endothelial cells", Proc. Natl. Acad. Sci. USA 91:3974-3978 | |
| | C03 | ANNABLE et al., 1972 'The Second International Reference Preparation of Erythropoietin, Human, Urinary, for Bioassay," Bull. Qrg. mond. Sante, 47:99-112. | |
| | C04 | ASHWELL et al., 1978, "A Protein from Mammalian Liver that Specifically Binds Galactose-Terminated Glycoproteins," Meth. Enzymol., 50:287-291. | |
| | C05 | BAUER, 1995, The Oxygen Sensor That Controls EPO Production: Facts and Fancies," J. Perinat. Med., 23:7-12. | |
| | C06 | BENYO et al., 1999, "Expression of erythropoietin receptor by trophoblast cells in the human placenta", Biol. Reproduct. 60:861-870 | |
| | C07 | BERN UDIN et al., 1999, "A potential role for erythropoietin in focal permanent cerebral ischemia in mice", J. Cereb. Blood Flow Metab. 19:643-651 | |
| | C08 | BERNAUDIN et al., 2000, "Neurons and astrocytes express EPO mRNA: oxygen-sensing mechanisms that involve the redox-state of the brain", Glia 30:271-278 | |
| • | C09 | BONDY, 1995, "The relaxation of oxidative stress and hyperexcitation to neurological disease", Proc. Soc. Exp. Biol. Med. 208:337-345 | |

| EXAMINER | |
|---------------|--|
| NYI-39/2311v2 | |

^{*}DXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

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| LICT OF AFFERENCES CITED BY ADDITIONT | ATTY. DOCKET NO. 10165-037-999 | APPLICATION NO. 10/520,140 (National Stage of PCT/US2003/021350) |
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| | | NON PATENT LITERATURE DOCUMENTS | |
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| Examiner | | | Τ |
| Initials | <u> </u> | (Include name of the author (in CAPITAL LETTERS), Title, Date, Pertinent Pages, Etc.) | T |
| | C10 | BRIGGS et al., 1974, "Hepatic Clearance of Intact and Desialylated Erythropsietin," Am. J. Physiol., 227:1385-1388. | |
| | C11 | BRINES et al., 2000, "Erythropoietin crosses the blood-brain barrier to protect against experimental brain injury", Proc. Natl. Acad. Sci. USA 97:10526-10531 | |
| | C12 | BRUNEVAL et al., 1993, "Erythropoietin Synthesis by Tumor Cells in a Case of Meningioma Associated With Erythrocytosis," Blood, 81, 593-1597. | |
| | C13 | CAMISCOLI et al., 1968, "Comparative Assay of Erythropoietin Standards," Annals New York Acad. Sci., 149:40-45. | † |
| | C14 | CAMPANA et al., 1998, "Identification of a neurotrophic sequence in erythropoietin", Int. J. Mol. Med. 1:235- | 1 |
| | C15 | CLAUS-WALKER et al., 1984, "Spinal Cord Injury and Serum Erythropoietin," Arch. Phys. Med. Rehabil., 65:370-374. | |
| | C16 | COTES, 1968, "Quantitative Estimation of Erythropoletin," Part I. Assay and Standardization of Erythropoletin, Annals New York Acad. Sci., 149:12-17. | |
| | C17 | COTES et al., 1961, "Bio-Assay of Erythropoietic in Mice Made Polycythaemic By Exposure to Air at a Reduced Pressure," Nature, 191:1065-1067. | |
| | C18 | COTES et al., 1966, "The International Reference Preparation of Erythropoietin," Bull. Org. mond. Sante, 35:751-760. | |
| | C19 | DIAZ-BRINTON et al., 1998, "Advance, and challenges in the prevention and treatment of Alzheimer's disease," Pharm. Res. 15(3):386-98 | |
| | C20 | DIGICAYLIOGLU et al. 1995, "Localization of specific crythropoietin binding sites in defined areas of the mouse brain.", Proc. Natl. Acad. Sat. USA 92:3717-3720 | |
| | C21 | DIPAOLO et al., 1992, "Effects of uremia and dialysis on brain electrophysiology after recombinant erythropoietin treatment", ASAO J. 38:M477-M480 | |
| | C22 | DONG et al., 1992, "Receptor binding of asialoerythropoietin," J. Cell. Biochem. 48(3):269-76 | |
| | C23 | DORDAL et al., 1985, "The Role of Carbohydrate in Erythropoietin Action," Endocrinol., 116:2293-2299. | |
| | C24 | DUBE et al, 1988, "Gl cosylation at Specific Sites of Erythropoietin is Essential for Biosynthesis, Secretion, and Biological Function," J. Biol. Chem., 263:17516-17521. | |
| | C25 | EHRENREICH et d., 2002, "Erythropoietin therapy for acute stroke is both safe and beneficial", Molec. Med. 8(8):495-505 | |
| | C26 | Eur. Pharmacopoeia, 1997, p. 5. | |
| | C27 | Eur. Pharmacopoeia, Suppl. 2001, pp. 777-782. | |
| | C28 | FARRELL et al., 2001, "Erythropoietin crosses the blood brain barrier", Blood 98:142b (abstr. # 4265; 43rd Annual Meeting of the American Society of Hematology, Orlando FL, Dec. 7-11, 2001) | |
| | C29 | FEIGIN et al., 2002, "Recent advances in Huntington's disease: implications for experimental therapeutics," Cur. Opin. Neurol. 15(4):483-9 | |
| | C30 | FUKUDA et al., 1989, "Survival of Recombinant Erythropoietin in the Circulation: The Role of Carbohydrates," Blood, 73:84-89. | |
| | C31 | GARTHOFF, 1995, "Safety and Efficacy Testing of Hormones and Related Products," The Report and | |

| EXAMINER |
|---------------|
| NYI-3972311v2 |

^{*}EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and no considered. Include copy of this form with next communication to applicant.

| N | | |
|---------------------------------------|------------------|---|
| | ATTY. DOCKET NO. | APPLICATION NO. 10/520,140 |
| | 10165-037-999 | |
| LIST OF REFERENCES CITED BY APPLICANT | | 101/032003/021330) |
| (Use several sheets if necessary) | APPLICANT | |
| | Brines et al. | 10/520,140 (National Stage of PCT/US2003/021350) |
| | FILING DATE | ATUNIT |
| | January 3, 2005 | /1647 |
| | | |

NON PATENT LITERATURE DOCUMENTS Examiner Initials (Include name of the author (in CAPITAL LETTERS), Title, Date, Pertinent Pages, Т Etc.) Recommendations of ECVAM Workshop 9, A.T.L.A., 23:699-711 GOLDWASSER et al., 1974, "On the Mechanism of Erythropoietin-Induced Differentiation," XIII. The Role of C32 Sialic Acid in Erythropoietin Action, J. Biol. Chem., 249:4202-4206. GOLDWASSER et al. 1975, "An Assay for Erythropoietin in Vitro at the Milliunit Level," Endo., 97:315-323. C33 GOLDWASSER et al., Crythropoietin: Assay and Study of Its Mode of Action," Hormone Assays, pp. 109-C34 121. GORIO et al., 2002, "Recombinant human erythropoietin counteracts secondary injury and markedly enhances C35 neurological recovery from experimental spinal cord trauma? Proc. Natl. Acad. Sci. USA 99:9450-9455 (PNAS Early Edition www.pnas.org/cgi/doi/10.1073/pnas.142287999) GRASSO et al., 2002, "Beneficial effects of systemic administration of recombinant human erythrpoietin in rabbits subjected to subarachnoid her orrhage", Proc. Matl. Acad. Sci. USA 99:5627-5631 C36 GREGORY et al., 1999, "GATA-1 and erythropoietic cooperate to promote erythroid cell survival by regulating C37 bcl-xL expression", Blood 94:87-96 GRIMM et al., 1990, "Improvement of brain function in hemodialysis patients treated with erythropoietin", C38 Kidney Intl. 38:480-486 HAMMOND et al., 1968, "Production, Utilian on and Excretion of Erythropoietin: I. Chronic Anemias. II. C39 Aplastic Crisis. III. Erythropoietic Effects of Normal Plasma," Erythropoietin, 149:516-527. HEFTI, 1997, "Pharmacology of neurotrophic factors", Annu. Rev. Pharmacol. Toxicol. 37:239-267 C40 HENGEMIHLE et al., 1996, "Chronic treatment with human recombinant erythropoietin increases hematocrit C4·1 and improves water maze performance in mice", Physio. Behav. 59:153-156 HIRAKATA et al., 1992, "CBF and oxygen metabolism in hemodialysis patients: effects of anemia correction with recombinant human EPO" Am. J. Physiol. 262:F737-F743 C42 HORTON et al., 1991, "Von Hippel-Lindau Disease and Erythrocytosis: Radioimmunoassay of Erythropoietin C43 in Cyst Fluid From a Brainstem Hemangioblastoma," Neurology 41:753-754. IMAI et al., 1990, "Physicochemical and Biological Characterization of Asialoerythropoietin," Eur. J. Biochem., C44 194:457-462. JOOSS et al., 1996, "Cyclophosphamide diminishes inflammation and prolongs transgene expression following C45 delivery of adenoviral vectors to mouse liver and lung," Hum. Gene The 7(13):1555-66 JUNK et al., 2007, "Erythropoietin administration protects retinal neurons from acute ischemia-reperfusion C46 injury", Proc. Natl. Acad. Sci. USA 99:10659-10664 (PNAS Early Edition www.pnas.or_/cgi/doi/10.1073/pnas.152321399) JUUL et al 1998, "Erythropoietin and erythropoietin receptor in the developing human central nervous C47 system", Jediatr. Res. 43:40-49 JUUL al., 1998, "Tissue distribution of erythropoietin and erythropoietin receptor in the developing human C48 fetus, Early Human Devel. 52:235-249 JUL et al., 2001, "Recombinant erythropoietin (EPO) crosses the blood brain barrier (ABB) in preterm fetal C49 skeep", Soc. for Neuroscience Abstracts 27:929 (31st Annual Meeting of the Society for Neuroscience, San Diego, CA Nov. 10-15, 2001) KEIGHLEY, 1968, "Further Experiences with Assays, Units, and Standards of Erythropoietin," Annals New York Acad. Sci., 149:18-24.

| EXAM I | ŀ | CR |
|---------------------|---|------|
| EXAMUN NYI-39/23 | l | l v2 |

^{*}EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not onsidered. Include copy of this form with next communication to applicant.

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| N . | | <i>y</i> |
|---------------------------------------|---|---|
| | ATTY. DOCKET NO. | APPLICATION NO. 10/520,140 (National Stage of |
| LIST OF REFERENCES CITED BY APPLICANT | 10103-037-333 | 1101/032093/021330) |
| (Use several sheets if necessary) | APPLICANT | |
| | 10/520,140 (National Stage of PCT/US2003/021350) | |
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| | | NON PATENT LITERATURE DOCUMENTS | |
|----------|----------|---|----------|
| Examiner | | | Γ_ |
| Initials | | (Include name of the author (in CAPITAL LETTERS), Title, Date, Pertinent Pages, Etc.) | T |
| | C51 | KOHAMA et al. 2000, "Large Uterine Myoma with Erythropoietin Messenger RNA and Erythrocytosis," | |
| | + | Obstetrics and Grecology, 96:826-828. KONISHI et al., 1933, "Trophic effect of crythropoietin and other hematogoietic factors on central cholinergic | ₩ |
| | C52 | | |
| | | neurons in vitro and it vivo", Brain Res. 609:29-35 KOPF et al., 1994, "Menory improving actions of glucose: involvement of a central cholinergic muscarinic | - |
| | C53 | mechanism.", Behav. Neural Biol. 62:237-243 | |
| | | LATINI et al., 1998, "Comparative efficacy of a DA2/α2 agonist and a β blocker in reducing adrenergic drive | \vdash |
| | C54 | and cardiac fibrosis in an experimental model of left ventricular sysfunction after coronary artery occlusion", J. | i |
| | | Cardiovasc. Pharmacol. 31:601–608 | |
| | 0.55 | LI et al., 1996, "Erythropoietin receptors are expressed in the central nervous system of mid-trimester human | ┼─ |
| | C55 | fetuses", Pediatr. Res. 40:376-380 | |
| | C56 | LI et al., 1998, "A single pre training ducose injection induces memory facilitation in rodents performing | \vdash |
| | C36 | various tasks: contribution of acidic fibrablast growth factor", Neurosci. 85:785-794 | |
| | C57 | LIPINSKI et al., 1995, "Nerve growth factor facilitates conditioned taste aversion learning in normal rats", Brain | T |
| | (37 | Res. 692:143-153 | |
| | C58 | LIU et al., 1996, "Transgenic mice containing the human erythropoietin receptor gene exhibit correct | T |
| | 1036 | hematopoietic and neural expression", Proc. Assoc. Am. Physicians 108:449-454 | |
| | C59 | LIU et al., 1997, "Regulated human erythrosoietin receptor expression in mouse brain", J. Biol. Chem. | T |
| | | 272:32395-32400 | |
| | C60 | LIU et al., 1994, "Tissue specific expression of human erythropoietin receptor in transgenic mice", Devel. Biol. | T |
| | | 166:159-169 | |
| | C61 | LOWY et al., 1960, "Inactivation of Erythropoietin by New aminidase and by Mild Substitution Reactions," | |
| | | Nature, 185:102-103. | |
| | C62 | MARRERO et al., 1998, "Erythropoietin receptor-operated Can+ channels: activation by phospholipase C-γ1", | |
| | | Kidney Intl. 53:1259-1268 | |
| | C63 | MARSH et al., 1991, "rHug PO treatment improves brain and cognitive function of anemic dialysis patients", | |
| | | Kidney Intl. 39:155-163 | |
| | C64 | MARTI et al., 1997, "Detection of erythropoietin in human liquor: intrinsic erythropoietin production in the | |
| | | brain", Kidney Intl. \$1:416-418 | L |
| | C65 | MARTI et al., 1996, "Erythropoietin gene expression in human, monkey and murine brain", Eur. J. Neurosci. | |
| | | 8:666-676 | 1_ |
| | C66 | MASUDA et 3t., 1997, "Insulin like growth factors and insulin stimulate erythropoietin production in primary | |
| | | cultured astrocytes", Brain Res. 746:63-70 | ┖ |
| | C67 | MASUDA et al., 1994, "A novel site of erythropoietin production. Oxygen dependent production in cultured rat | |
| | | astrocytes", J. Biol. Chem. 269:19488-19493 | ╙ |
| | C68 | MASUDA et al., 1993, "Functional erythropoietin receptor of the cells with neural characteristics. Comparison | |
| | | with receptor properties of erythroid cells", J. Biol. Chem. 268:11208-11216 | _ |
| | C69 | MATSUYAMA et al., 2000, "Erythrocytosis Caused by an Erythropoietin-Producing Hepatocellular | |
| | - | Zarcinoma," J. Surg. Oncology, 75:197-202. | |
| | C70 | MIONI et al., 1992, "Evidence for specific binding and stimulatory effects of recombinant human erythropoietin | |
| | | on isolated adult rat Leydig cells", Acta Endocrinologica 127:459-465 | |

| EXAMI X ER |
|-------------------|
| NYI-39/2311v2 |

^{*}FXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

| | ATTY. DOCKET NO. | APPLICATION NO. 10/520,140 (National Stage of |
|---------------------------------------|------------------|---|
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| (Use several sheets if necessary) | APPLICANT | |
| | Brines et al. | |
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| NON PATENT LITERATURE DOCUMENTS | | | |
|---------------------------------|-----|--|-----|
| Examiner nitials | | (Include name of the author (in CAPITAL LETTERS), Title, Date, Pertinent Pages Actc.) | Т |
| illiais | C71 | MIYAKE et al., 1977, "Purification of Human Erythropoietin," J. Biol. Chem., 252:5558-5564. | + 1 |
| | C72 | MORELL et al., 1368, "Physical and Chemical Studies on Ceruloplasmin," Metabolic Studies on Sialic Acid- Free Ceruloplasmin in Vivo, J. Biol. Chem., 243:155-159. | |
| | C73 | MORISHITA et al., 1907, "Erythropoietin receptor is expressed in rat hippocampal and cerebral cortical neurons, and erythropoietin prevents in vitro glutamate induced neuronal death", Neurosci. 76:105-116 | |
| | C74 | MOSS et al., 1996, "Oxygen administration enhances memory fornation in healthy young adults", Psychopharmacol. 124:255-260 | |
| | C75 | NAKAMURA et al., 1998, "Elevated levels of erythropoietin in cerebrospinal fluid of depressed patients", Am. J. Med. Sci. 315:199-201 | |
| | C76 | NISSENSON et al., 1991, "Recombinant human erythrop letin and renal anemia: molecular biology, clinical efficacy and nervous system effects", Ann. Int. Med. 114:402-416 | |
| | C77 | NISSENSON, 1989, "Recombinant hunan erythropoietin: impact on brain and cognitive function, exercise tolerance, sexual potency and quality of Me", Sem. Nephrol. 9(suppl. 2):25-31 | |
| | C78 | OGDEN, 1989, "Monitoring consideration in recombinant human erythropoietin therapy", Sem. Nephrol. 9(suppl. 2):12-15 | |
| | C79 | OKADA et al., 1996, "Erythropoietin stimulates proliferation of rat-cultured gastric mucosal cells", Digestion 57:328-332 | |
| | C80 | PARDRIDGE, 1997, "Drug delivery to the brain", Cerebral Blood Flow Metab. 17:713-731 | T |
| | C81 | PARDRIDGE et al., 1991, "Selective transport of an arti-transferrin receptor antibody through the blood-brain barrier in vivo", J. Pharmacol. Exp. Ther. 27:66-70 | T |
| | C82 | PLAPP et al., 1971, "Activity of bovine pancreatic deoxyrbonuclease A with modified amino groups," J. Biol. Chem. 246(4):939-45 | |
| | C83 | PODUSLO et al., 1994, "Macromolecular premeability across the blood-nerve and blood-brain barriers", Proc. Natl. Acad. Sci. USA 91:5705-5709 | |
| | C84 | PRENDERGAST et al., 1997, "Nitric oxide synthase inhibition impairs spatial navigation learning and induces conditioned taste aversion", Pharmacol. Biochem. Behav. 57:347-35 | Γ |
| | C85 | ROBINSON et al., 1975, "Tetanus toxin. The effect of chemical modifications on toxicity, immunogenicity, and conformation," J. Bjøl. Chem. 250(18):7435-42 | |
| | C86 | ROSE et al., 1998 "Receptor-mediated angiotensin II transcytosis by brain microvessel endothelial cells", Peptides 19:102-1030 | |
| | C87 | SADAMATO et al., 1998, "Erythropoietin prevents place navigation disability and cortical infarction in rats with permanent occlusion of the middle cerebral artery", Biochem. Biophys. Res. Comm. 253:26-32 | |
| | C88 | SAKANAKA et al., 1998, "In vivo evidence that erythropoietin protects neurons from ischemic damage", Proc. Natl. Acad. Sci. USA 95:4635-4640 | |
| | C89 | SATARE et al. 1990, "Chemical modification of erythropoietin: an increase in in vitro ctivity by guaridination," Biochim. Biophys. Acta. 1038(1):125-9 | |
| | C90 | SAWYER et al., 1989, "Receptors for erythropoietin in mouse and human erythroid cells and placenta", Blood 4:103-109 | |
| | C91 | SHIRAMIZU et al., 1994, "Constitutive Secretion of Erythropoietin by Human Renal Adenocal cinoma Cells in Vivo and in Vitro," Exp. Cell Res., 215:249-256. | 1 |

EXAMPLER NYI-39/2311v2

^{*}FXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and include the conf onsidered. Include copy of this form with next communication to applicant.

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| LIST OF REFERENCES CITED BY APPLICANT | 10165-037-999 | PCT/US29/03/021350) |
| (Use several sheets if necessary) | APPLICANT | |
| | Brines et al. | |
| | FILING DATE | ARZ UNIT |
| | January 3, 2005 | 1647 |

NON PATENT LITERATURE DOCUMENTS Examiner Initials (Include name of the author (in CAPITAL LETTERS), Title, Date, Pertinent Pages, Т SHORE et al., 1968, "Quantitative Estimation of Erythropoietin," Annals New York Acad. Sci., 149:46-48. C92 SILVA et al., 1998 "Erythropoietin can induce the expression of bel-xL through Stat5 in erythropoietin-C93 dependent progenito cell lines", J. Biol. Chem. 274:22165-22169 SIRÉN et al., 2001, "Bythropoietin prevents neuronal apoptosis after gerebral ischemia and metabolic stress", C94 Proc. Natl. Acad. Sci. USA 98:4044-4049 SPIVAK et al., 1989, "The In Vivo Metabolism of Recombinant Human Erythropoietin in the Rat," Blood, C95 73:90-99. STARK et al., 1960, "Reactions of the Cyanate Present in Aqueous Urea With Amino Acids and Proteins," J. C96 Biol. Chem. 235(11): 3177-318 STEECE-COLLIER et al., 2002, "Etiology of Parkinson's disease: Genetics and environment revisited," Proc. C97 Natl. Acad. Sci. U. S. A. 99(22):139 2-4 STORRING et al., 1998, "Epoietin Alia and Beta Differ In Erythropoietin Isoform Compositions and Biological C98 Properties," British J. Haematology, 100 79-89. STORRING et al., 1992, "The International Standard for Recombinant DNA-Derived Erythropoietin: C99 Collaborative Study of Four Recombinant DNA derived Erythropoietins and Two Highly Purified Human **(**59-484. Urinary Erythropoietins," J. Endocrinol., 134 SUZUKI et al., 2001, "Erythropoietin Synthesis by Tumour Tissues in a Patient With Uterine Myoma and C100 ERythrocytosis," British J. Haematology, 13:49-3 TABIRA et al., 1995, "Neurotrophic effect of hematopoietic cytokines on cholinergic and other neurons in C101 vitro", Int. J. Devl. Neurosci. 13:241-2 WEILAND et al., "In vivo Activity of Asialo-Erythropoletin in Combination with Asialo-Glycoproteins," 1982, C102 Blut, 44:173-175. WESTENFELDER et al., 1999 Human, rat and mouse kidney cells express functional erythropoietin C103 receptors", Kidney Intl. 55:80 -820 WILLIAMS et al., 1994, "Haman erythropoietin receptor", Ann. NY Acad. Sci. 718:232-244 C104 WOLCOTT et al., 1989, Recombinant human erythropoietin treatment may improve quality of life and C105 cognitive function in chronic hemodialysis patients", Am. J. Kidney Dis. 14:478-485 WU et al., 1999, "Nedroprotection with noninvasive neurotrophin delivery to the brain", PNAS 96:254-259 C106 YAMAJI et al., 1996, "Brain capillary endothelial cells express two forms of erythropoietin receptor mRNA", C107 Eur. J. Biochem 239:494-500 YANG et al., 2002, "Effects of ammonia and glucosamine on the heterogeneity of erythropoietin glycoforms," C108 Biotechnol. Frog. 18(1):129-38

EXAMINER NYI-39**7**2311v2

^{*}EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and lot considered. Include copy of this form with next communication to applicant.

LIST OF REFERENCES CITED BY APPLICANT
(Use several sheets if necessary)

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APPLICATION NO. 10/520,140
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U.S. PATENT DOCUMENTS

| | I | 1 | | T | PAGES, COLUMNS, LINES, WHERE |
|----------------------|-----|-----------------|----------|------------------|---|
| *EXAMINER INITIAL | | DOCUMENT NUMBER | DATE | NAME | RELEVANT PASSAGES OR RELEVANT FIGURES APPEAR |
| | A01 | 4,377,513 | 03/22/83 | Sugimoto et al. | |
| | A02 | 4,703,008 | 10/27/87 | Lin | |
| | A03 | 4,806,524 | 02/21/89 | Kawaguchi et al. | |
| | A04 | 4,835,260 | 05/30/89 | Shoemaker | |
| | A05 | 5,457,089 | 10(10/95 | Fibi et al. | |
| | A06 | 5,547,933 | 08/20/96 | Lin | |
| | A07 | 5,571,787 | 11/05/98 | O'Brien et al. | |
| | A08 | 5,614,184 | 03/25/97 | Sytkowski et al. | |
| | A09 | 5,618,698 | 04/08/97 | in | |
| | A10 | 5,621,080 | 04/15/97 | Li | |
| | A11 | 5,625,035 | 04/29/97 | Clemens | |
| | A12 | 5,661,125 | 08/26/97 | Strickland | |
| | Λ13 | 5,696,080 | 12/09/97 | Ø' Brien | |
| | A14 | 5,700,909 | 12/23/97 | O'Brien | |
| | A15 | 5,714,459 | 02/03/98 | O'Brien | |
| | A16 | 5,756,349 | 05/26/98 | Lin | |
| | A17 | 5,767,078 | 06/16/98 | Johnson et al. | |
| | A18 | 5,773,569 | 6/30/98 | Wrighton et al. | |
| | A19 | 5,830,851 | 11/03/98 | Wrighton et al. | |
| | A20 | 5,835,382 | 11/10/98 | Wilson et al. | |
| | A21 | 5,856,298 | 01/05/99 | Strickland | |
| | A22 | 5,888,772 | 03/30/99 | Okasinski et al. | |
| | A23 | 5,955,422 | 09/21/99 | Lin | |
| | A24 | 6,165,783 | 12/26/00 | Weiss et al. | |
| | A25 | 4,658,919 | 04/14/87 | Kung et al. | 1 |

FOREIGN PATENT DOCUMENTS

EXAMINER NYI-3972611v2

^{*}EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and to considered. Include copy of this form with next communication to applicant.

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| LIST OF REFERENCES CITED BY APPLICANT | ATTY. DOCKET NO. 10165-037-999 | APPLICATION NO. 10/520,140 (National Stage of PCT/US2003/021350) |
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| | POREIGN PATENT DOCUMENT COUNTRY CODE, NUMBER, KIND CODE (IF KNOWN) | DATE | NAME | PAGES, COLUMNS, LINES, WHERE RELEVANT PASSAGES OR RELEVANT FIGURES APPEAR | Т |
| B01 | JP 5-24688 | 09/24/93 | JP-A Kokai | | |
| B02 | WO 94/24160 | 10/27/94 | Brigham and Women's Hospital | | |
| B03 | WO 95/05465 | 02/23/95 | Amgen, Inc. | | |
| B04 | WO 97/18318 | 05/22/97 | Takara Shuzo Co., Ltd. | | |
| B05 | WO 97/32895 | 12/12/97 | Regents of the University of California | | |
| B06 | WO 98/18926 | 5/07/98 | G.D. Searle & Co. | | |
| B07 | WO 00/35475 | 06/22/00 | Ehrenreich | | |
| B08 | WO 01/82952 | 11/08%01 | Action Pharma APS | | |
| B09 | WO 01/82953 | 11/08/0 | Action Pharma APS | | |
| B10 | EP 555880 | 08/18/93 | Bristol-Myers Squibb Company | | |
| B11 | WO 92/08493 | 5/29/92 | Brigham & Women's Hospital | | |
| B12 | WO 96/14081 | 5/17/96 | Boehringer Manheim gmbh | | |
| B13 | WO 02/10743 | 2/07/02 | Ortho McNeil Pharmaceutical, Inc. | | |

| Examiner | | | |
|----------|-----|---|---|
| Initials | | (Include name of the author (in CAP/TAL LETTERS), Title, Date, Pertinent Pages, Etc.) | Т |
| | C01 | ALAFACI et al., 2000, "Effect of Recombinant Human Ery proposetin on Cerebral Ischemia Following Experimental Subarachnoid Homorrhage," Eur. J. Phar., 406:249-225. | |
| | C02 | ANAGNOSTOU et al., 1994 "Erythropoietin receptor mRNA expression in human endothelial cells", Proc. Natl. Acad. Sci. USA 91:374-3978 | |
| | C03 | ANNABLE et al., 1972, The Second International Reference Preparation of Erythropoietin, Human, Urinary, for Bioassay," Bull. Org. mond. Sante, 47:99-112. | |
| | C04 | ASHWELL et al., 1978, "A Protein from Mammalian Liver that Specifically Binds Galactose-Terminated Glycoproteins," Moth. Enzymol., 50:287-291. | |
| | C05 | BAUER, 1995, "The Oxygen Sensor That Controls EPO Production: Facts and Fancies," J. Perinat. Med., 23:7-12. | |
| | C06 | BENYO et al., 1999, "Expression of erythropoietin receptor by trophoblast cells in the human placenta", Biol. Reproduct, 60:861-870 | |
| | C07 | BERNAL DIN et al., 1999, "A potential role for erythropoietin in focal permanent carebral ischemia in mice", J. Cereb, Blood Flow Metab. 19:643-651 | |
| | C08 | BERNAUDIN et al., 2000, "Neurons and astrocytes express EPO mRNA: oxygen-sensing mechanisms that involve the redox-state of the brain", Glia 30:271-278 | |
| | C09 | PONDY, 1995, "The relaxation of oxidative stress and hyperexcitation to neurological disease", Proc. Soc. Exp. Biol. Med. 208:337-345 | |

| | · | * |
|---------------------------|-----------------|---|
| EXAMINER NY1-3977311v2 | DATE CONSIDERED | |

^{*}EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

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| | | ATTY. DOCKET NO. | APPLICATION NO. 10/520,140 (National Stage of |
| LIST OF REFERENCES CITED BY APPLICANT | | 10165-037-999 | PCT/US2 \$ 03/021350) |
| (Use several sheets if necessary) | | APPLICANT | |
| | | Brines et al. | |
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| | NON PATENT LITERATURE DOCUMENTS | |
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| Examiner | (Include new defithe author (in CADITAL LETTERS) Title Date Partie ant Page (to) | Т |
| Initials C10 | (Include name of the author (in CAPITAL LETTERS), Title, Date, Pertinent Pages Etc.) BRIGGS et al., 1974, "Hepatic Clearance of Intact and Desialylated Erythropoietin," Am. J. Physiol., 227:1385-1388. | |
| CII | | |
| C12 | BRUNEVAL et al., 1993, "Erythropoietin Synthesis by Tumor Cells in a Case of Meningioma Associated With Erythrocytosis," Blood, 8 : 1593-1597. | |
| C13 | 149:40-45. | |
| C14 | CAMPANA et al., 1998, "Identification of a neurotrophic sequence in erythropoietin", Int. J. Mol. Med. 1:235-241 | |
| CIS | 65:370-374. | |
| Cle | COTES, 1968, "Quantitative Estimation of Erythropaletin," Part I. Assay and Standardization of Erythropoletin, Annals New York Acad. Sci., 149:72-17. | |
| C17 | Reduced Pressure," Nature, 191:1065-1067. | |
| C18 | 35:751-760. | |
| C19 | disease," Pharm. Res. 15(3):386-98 | |
| C20 | DIGICAYLIOGLU et al. 1995, "Localization of specific crythropoietin binding sites in defined areas of the mouse brain.", Proc. Natl. Acad. Sci. USA 92:3717-3720 | |
| C21 | | |
| C22 | DONG et al., 1992, "Receptor binding of asialoerythropoietin," A Cell. Biochem. 48(3):269-76 | 1 |
| C23 | DORDAL et al., 1985, "The Role of Carbohydrate in Erythropoietin Action," Endocrinol., 116:2293-2299. | 1 |
| C24 | and Biological Function," J. Biol. Chem., 263:17516-17521. | |
| C2: | DUDENID FIGURE A COOR OF A LAND A LAN | |
| C26 | Eur. Pharmacopoeia, 1997, p. 5. | |
| C21 | Eur. Pharm copoeia, Suppl. 2001, pp. 777-782. | |
| C28 | FARRELL et al., 2001, "Erythropoietin crosses the blood brain barrier", Blood 98:148b (abstr. # 4265; 43rd Annual Meeting of the American Society of Hematology, Orlando FL, Dec. 7-11, 200 | |
| C29 | DELOGAL 1 2002 (CD | |
| C30 | | |
| C3 | C. P. T. 1. C. P. 1. | |

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^{*}EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

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| | ATTY. DOCKET NO. | APPLICATION NO. 10/520,140 |
| LIST OF REFERENCES CITED BY APPLICANT | 10165-037-999 | (National Stage of PCT/US2003/021350) |
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| • | | ar |

| | | NON PATENT LITERATURE DOCUMENTS | |
|----------------------|-----|--|---|
| Examiner Initials | | (Include name of the author (in CAPITAL LETTERS), Title, Date, Pertinent Pages, Fic.) Recommendations of ECVAM Workshop 9, A.T.L.A., 23:699-711 | Т |
| | C32 | GOLDWASSER et al., 1974, "On the Mechanism of Erythropoietin-Induced Differentiation," XIII. The Role of Sialic Acid in Erythropoietin Action, J. Biol. Chem., 249:4202-4206. | |
| | C33 | GOLDWASSER et al., 1975, "An Assay for Erythropoietin in Vitro at the Milliunit Level," Endo., 97:315-323. | |
| | C34 | GOLDWASSER et al., "Bythropoietin: Assay and Study of Its Mode of Action," Hormone Assays, pp. 109-121. | |
| | C35 | GORIO et al., 2002, "Recombinant human erythropoietin county acts secondary injury and markedly enhances neurological recovery from experimental spinal cord trauma" Proc. Natl. Acad. Sci. USA 99:9450-9455 (PNAS Early Edition www.pnas.org/cgi/dai/10.1073/pnas.14228789) | |
| | C36 | GRASSO et al., 2002, "Beneficial effects of systemic administration of recombinant human erythrpoietin in rabbits subjected to subarachnoid hemographe", Proc. Natl. Acad. Sci. USA 99:5627-5631 | |
| | C37 | GREGORY et al., 1999, "GATA-1 and rythropoietic cooperate to promote erythroid cell survival by regulating bcl-xL expression", Blood 94:87-96 | 1 |
| | C38 | GRIMM et al., 1990, "Improvement of brain function in hemodialysis patients treated with erythropoietin", Kidney Intl. 38:480-486 | |
| | C39 | HAMMOND et al., 1968, "Production, Utilization and Excretion of Erythropoietin: I. Chronic Anemias. II. Aplastic Crisis. III. Erythropoietic Effects of Normal Plasma," Erythropoietin, 149:516-527. | |
| | C40 | HEFTI, 1997, "Pharmacology of neurotrophic factor", Annu. Rev. Pharmacol. Toxicol. 37:239-267 | |
| | C41 | HENGEMIHLE et al., 1996, "Chronic treatment with human recombinant erythropoietin increases hematocrit and improves water maze performance in mice", Physiol. Behav. 59:153-156 | |
| | C42 | HIRAKATA et al., 1992, "CBF and oxygen metabolism in remodialysis patients: effects of anemia correction with recombinant human EPO" Am. J. Physiol. 262:F737-F743 | |
| | C43 | HORTON et al., 1991, "Von Vippel-Lindau Disease and Erythrocytosis: Radioimmunoassay of Erythropoietin in Cyst Fluid From a Brainsem Hemangioblastoma," Neurology, 11:753-754. | |
| | C44 | IMAI et al., 1990, "Physiochemical and Biological Characterization of Asialoerythropoietin," Eur. J. Biochem., 194:457-462. | T |
| | C45 | JOOSS et al., 1996, "Eyclophosphamide diminishes inflammation and prolongs transgene expression following delivery of adenovial vectors to mouse liver and lung," Hum. Gene Ther. 7(13):1555-66 | |
| | C46 | JUNK et al., 2007, "Erythropoietin administration protects retinal neurons from acute ischemia-reperfusion injury", Proc. Natl. Acad. Sci. USA 99:10659-10664 (PNAS Early Edition www.pnas.org/cgi/doi/10.1073/pnas.152321399) | |
| | C47 | JUUL et al. 1998, "Erythropoietin and erythropoietin receptor in the developing human central nervous system", Jediatr. Res. 43:40-49 | |
| | C48 | JUUL et al., 1998, "Tissue distribution of erythropoietin and erythropoietin receptor in the developing human fetus", Early Human Devel. 52:235-249 | |
| | C49 | JUDL et al., 2001, "Recombinant erythropoietin (EPO) crosses the blood brain barrier (BBB) in preterm fetal sleep", Soc. for Neuroscience Abstracts 27:929 (31st Annual Meeting of the Society for Neuroscience, San Diego, CA Nov. 10-15, 2001) | |
| | C50 | KEIGHLEY, 1968, "Further Experiences with Assays, Units, and Standards of Erythropoietin," Annals New York Acad. Sci., 149:18-24. | |

| EXAMINE | ₹ |
|--------------|----|
| NYI-3972311v | /2 |

^{*}XAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

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| (Use several sheets if necessary) | APPLICANT | |
| | Brines et al. | |
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| | | NON PATENT LITERATURE DOCUMENTS | |
|----------|-----|--|----------|
| Examiner | T | | Γ |
| Initials | | (Include name of the author (in CAPITAL LETTERS), Title, Date, Pertinent Pages Etc.) | T |
| | C51 | KOHAMA et al., 2000, "Large Uterine Myoma with Erythropoietin Messenger RNA and Erythrocytosis," | |
| | | Obstetrics and Gynecology, 96:826-828. | |
| | C52 | KONISHI et al., 1933, "Trophic effect of erythropoietin and other hemat poietic factors on central cholinergic neurons in vitro and it vivo", Brain Res. 609:29-35 | |
| | CE2 | KOPF et al., 1994, "Memory improving actions of glucose: involvement of a central cholinergic muscarinic | \vdash |
| | C53 | mechanism.", Behav. Neural Biol. 62:237-243 | |
| | C54 | LATINI et al., 1998, "Comparative efficacy of a DA2/α2 agonist and a β blocker in reducing adrenergic drive | |
| | | and cardiac fibrosis in an experimental model of left ventricular dysfunction after coronary artery occlusion", J. | 1 |
| | | Cardiovasc. Pharmacol. 31:601 608 | |
| | C55 | LI et al., 1996, "Erythropoietin receptors are expressed in the central nervous system of mid-trimester human | |
| | | fetuses", Pediatr. Res. 40:376-380 | |
| | C56 | LI et al., 1998, "A single pre training Jucose injection induces memory facilitation in rodents performing | Γ |
| | | various tasks: contribution of acidic fibroblast growtly factor", Neurosci. 85:785-794 | |
| | C57 | LIPINSKI et al., 1995, "Nerve growth factor facilitates conditioned taste aversion learning in normal rats", Brain | |
| | | Res. 692:143-153 | |
| | C58 | LIU et al., 1996, "Transgenic mice containing the human erythropoietin receptor gene exhibit correct | Γ |
| | | hematopoietic and neural expression", Proc. Assoc. Am. Physicians 108:449-454 | |
| | C59 | LIU et al., 1997, "Regulated human erythropoieting eceptor expression in mouse brain", J. Biol. Chem. | Γ |
| | | 272:32395-32400 | |
| | C60 | LIU et al., 1994, "Tissue specific expression of human crythropoietin receptor in transgenic mice", Devel. Biol. | Γ |
| | | 166:159-169 | L |
| | C61 | LOWY et al., 1960, "Inactivation of Erythropoietin by Newaminidase and by Mild Substitution Reactions," | |
| | | Nature, 185:102-103. | |
| | C62 | MARRERO et al., 1998, "Erytaropoietin receptor-operated Can+ channels: activation by phospholipase C-γ1", | |
| | | Kidney Intl. 53:1259-1268 | |
| | C63 | MARSH et al., 1991, "rHyEPO treatment improves brain and cognitive function of anemic dialysis patients", | |
| | _ | Kidney Intl. 39:155-163 | L |
| | C64 | MARTI et al., 1997, "Detection of erythropoietin in human liquor: intrasic erythropoietin production in the | |
| | | brain", Kidney Intl. \$1:416-418 | L |
| | C65 | MARTI et al., 1998, "Erythropoietin gene expression in human, monkey and murine brain", Eur. J. Neurosci. | 1 |
| | | 8:666-676 | L |
| | C66 | MASUDA et a., 1997, "Insulin like growth factors and insulin stimulate erythropoietin production in primary | |
| | | cultured astrocytes", Brain Res. 746:63-70 | |
| | C67 | MASUDA et al., 1994, "A novel site of erythropoietin production. Oxygen dependent production in cultured rat | ĺ |
| | | astrocytes", J. Biol. Chem. 269:19488-19493 | L |
| | C68 | MASUDA et al., 1993, "Functional erythropoietin receptor of the cells with neural characteristics. Comparison | Γ |
| | | with receptor properties of erythroid cells", J. Biol. Chem. 268:11208-11216 | L |
| | C69 | MATSUYAMA et al., 2000, "Erythrocytosis Caused by an Erythropoietin-Producing Heparocellular | |
| | | Carcinoma," J. Surg. Oncology, 75:197-202. | |
| | C70 | MIONI et al., 1992, "Evidence for specific binding and stimulatory effects of recombinant human erythropoietin | |
| | | on isolated adult rat Leydig cells", Acta Endocrinologica 127:459-465 | |

| EXAMINER |
|------------------------|
| NYI-39 7 2311v2 |

^{*}EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

| | ATTY. DOCKET NO. | APPLICATION NO. 10/520,140 |
|---|------------------|---------------------------------------|
| LIST OF REFERENCES CITED BY APPLICANT (Use several sheets if necessary) | 10165-037-999 | (National Stage of PCT/US2007/021350) |
| | APPLICANT | |
| | Brines et al. | |
| | FILING DATE | ARTINIT |
| | January 3, 2005 | 1947 |
| A | | AF |

NON PATENT LITERATURE DOCUMENTS Examiner Initials (Include name of the author (in CAPITAL LETTERS), Title, Date, Pertinent Pages, Ex Т MIYAKE et al., 1977, "Purification of Human Erythropoietin," J. Biol. Chem., £52:5558-5564. C71 MORELL et al., 1968, "Physical and Chemical Studies on Ceruloplasmin," Metabolic Studies on Sialic Acid-C72 Free Ceruloplasmin N Vivo, J. Biol. Chem., 243:155-159. MORISHITA et al., 1997, "Erythropoietin receptor is expressed in rat hippocampal and cerebral cortical C73 neurons, and erythropoieth prevents in vitro glutamate induced neuronal death", Neurosci. 76:105-116 MOSS et al., 1996, "Oxygen administration enhances memory formation in healthy young adults", C74 Psychopharmacol. 124:255-260 NAKAMURA et al., 1998, "Elevated levels of erythropoietin in cerebrospinal fluid of depressed patients", Am. C75 J. Med. Sci. 315:199-201 NISSENSON et al., 1991, "Recombigant human erythropojetin and renal anemia: molecular biology, clinical C76 efficacy and nervous system effects", Ann. Int. Med. 114;402-416 NISSENSON, 1989, "Recombinant human erythropoies"n: impact on brain and cognitive function, exercise C77 tolerance, sexual potency and quality of life", Sem. Nephrol. 9(suppl. 2):25-31 OGDEN, 1989, "Monitoring considerations to recombinant human erythropoietin therapy", Sem. Nephrol. C78 9(suppl. 2):12-15 OKADA et al., 1996, "Erythropoietin stimulates proliferation of rat-cultured gastric mucosal cells", Digestion C79 57:328-332 PARDRIDGE, 1997, "Drug delivery to the orain", J. Cerebral Blood Flow Metab. 17:713-731 C80 PARDRIDGE et al., 1991, "Selective transport of an anti-transferrin receptor antibody through the blood-brain C81 barrier in vivo", J. Pharmacol. Exp. Tyer. 27:66-70 PLAPP et al., 1971, "Activity of boyine pancreatic deoxyrib nuclease A with modified amino groups," J. Biol. C82 Chem. 246(4):939-45 PODUSLO et al., 1994, "Macromolecular premeability across the blood-nerve and blood-brain barriers", Proc. C83 Natl. Acad. Sci. USA 91:570 -5709 PRENDERGAST et al., 1997, "Nitric oxide synthase inhibition impairs spatial navigation learning and induces C84 conditioned taste aversion, Pharmacol. Biochem. Behav. 57:347-352 ROBINSON et al., 1978, "Tetanus toxin. The effect of chemical modifications on toxicity, immunogenicity, and C85 conformation," J. Big. Chem. 250(18):7435-42 ROSE et al., 1998, Receptor-mediated angiotensin II transcytosis by brain nicrovessel endothelial cells", C86 Peptides 19:1023/1030 SADAMATO At al., 1998, "Erythropoietin prevents place navigation disability and cortical infarction in rats C87 with permanent occlusion of the middle cerebral artery", Biochem. Biophys. Res. comm. 253:26-32 SAKANAKA et al., 1998, "In vivo evidence that erythropoietin protects neurons from ischemic damage", Proc. C88 Natl. Acad. Sci. USA 95:4635-4640 SATAXE et al. 1990, "Chemical modification of erythropoietin: an increase in in vitro activity by C89 guan dination," Biochim. Biophys. Acta. 1038(1):125-9 SAWYER et al., 1989, "Receptors for erythropoietin in mouse and human erythroid cells and placenta", Blood C90 **4**:103-109 SHIRAMIZU et al., 1994, "Constitutive Secretion of Erythropoietin by Human Renal Adenocarc groma Cells in C91 Vivo and in Vitro," Exp. Cell Res., 215:249-256.

EXAMINER NYI-39/2311v2

^{*}JXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

| 8 | | |
|---|---------------------------------|--|
| LIST OF REEDENICES CITED DV ADDITIONIT | ATTY. DOCKET NO. 10165-037-999 | APPLICATION NO. 10/520,140 (National Stage of PCT/US2002/021350) |
| LIST OF REFERENCES CITED BY APPLICANT (Use several sheets if necessary) | APPLICANT | |
| (Osc several sheets if necessary) | Brines et al. | |
| | Diffies et al. | |
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| • | | NON PATENT LITERATURE DOCUMENTS | |
|----------|------|---|------------------|
| Examiner | | (Include any Sales without Co. CADITAL LETTERS). Title Date Designation of Date | Т |
| Initials | C92 | (Include name of the author (in CAPITAL LETTERS), Title, Date, Pertinent Pages, Etc.) SHORE et al., 1968, "Quantitative Estimation of Erythropoietin," Annals New York Acad. Sci., 149:46-48. | ' - |
| | 1 | SILVA et al., 1999, "Erythropoietin can induce the expression of bcl-xL through Stat5 in erythropoietin- | 1 |
| | C93 | dependent progenitor cell lines", J. Biol. Chem. 274:22165-22169 | |
| | C94 | SIRÉN et al., 2001, "En thropoietin prevents neuronal apoptosis after cerebral ischemia and metabolic stress", | |
| | C95 | Proc. Natl. Acad. Sci. USA 98:4044-4049 SPIVAK et al., 1989, "The in Vivo Metabolism of Recombinant Human Erythropoietin in the Rat," Blood, | <u> </u> |
| | C93 | 73:90-99. | |
| | C96 | STARK et al., 1960, "Reactions of the Cyanate Present in Aqueous Urea With Amino Acids and Proteins," J. Biol. Chem. 235(11): 3177-3181 | |
| | C97 | STEECE-COLLIER et al., 2002, "Exiology of Parkinson's disease: Genetics and environment revisited," Proc. Natl. Acad. Sci. U. S. A. 99(22):1397-4 | |
| | C98 | STORRING et al., 1998, "Epoietin Alfa and Beta Differ in Erythropoietin Isoform Compositions and Biological Properties," British J. Haematology, 100: 2-89. | |
| | C99 | STORRING et al., 1992, "The International Standard for Recombinant DNA-Derived Erythropoietin: Collaborative Study of Four Recombinant DNA-derived Erythropoietins and Two Highly Purified Human Urinary Erythropoietins," J. Endocrinol., 134:439-484. | |
| | C100 | 7 W | |
| | C101 | TABIRA et al., 1995, "Neurotrophic effect of hematopoietic cytokines on cholinergic and other neurons in vitro", Int. J. Devl. Neurosci. 13:241-252 | |
| | C102 | T | |
| | C103 | WESTENFELDER et al., 1999, "Human, rat and mouse kidne cells express functional erythropoietin receptors", Kidney Intl. 55:808,820 | |
| | C104 | | |
| | C105 | WOLCOTT et al., 1989, "Recombinant human erythropoietin treatment may improve quality of life and cognitive function in chronic hemodialysis patients", Am. J. Kidney Dis 14:478-485 | |
| | C106 | | |
| | C107 | Eur. J. Biochem 239:494-500 | |
| | C108 | YANG et al., 2002, "Effects of ammonia and glucosamine on the heterogeneity of erythropoietin glycoforms," Biotechnol. Prog. 18(1):129-38 | |

EXAMINER NYI-39**72**311v2

^{*}EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

10520140 - GAU: 164 Express Mail No.: DRAFT Sheet I of 7 of List of References

APPLICATION NO. ATTY. DOCKET NO. 10/520,140 (National Stage of PCT/US2903/021350) 10165-037-999 LIST OF REFERENCES CITED BY APPLICANT (Use several sheets if necessary) APPLICANT Brines et al. AP UNIT FILING DATE 647 January 3, 2005

| TICI | PATENT | DOCIIN | MENTE |
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| | | | U.S. PA | STENT DOCUMENTS | |
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| *EXAMINER INITIAL | | DOCUMENT NUMBER | DATE | NAME | PAGES, COLUMNS, LINES, WHERE RELEVANT PASSAGES OR RELEVANT FIGURES APPEAR |
| | A01 | 4,377,513 | 03/22/83 | Sugimoto et al. | |
| | A02 | 4,703,008 | 10/27/87 | Lin | |
| | A03 | 4,806,524 | 02/21/89 | Kawaguchi et al. | |
| | A04 | 4,835,260 | 05/30/89 | Shoemaker | |
| | A05 | 5,457,089 | 10010/95 | Fibi et al. | |
| · | A06 | 5,547,933 | 08/20/96 | Lin | |
| | A07 | 5,571,787 | 11/05/90 | O'Brien et al. | |
| | A08 | 5,614,184 | 03/25/97 | Sytkowski et al | |
| | A09 | 5,618,698 | 04/08/97 | in | |
| | A10 | 5,621,080 | 04/15/97 | Lin | |
| | All | 5,625,035 | 04/29/97 | Clemos | |
| | A12 | 5,661,125 | 08/26/97 | Strickland | |
| | A13 | 5,696,080 | 12/09/97 | Brien | |
| | A14 | 5,700,909 | 12/23/97 | O'Brien | |
| | A15 | 5,714,459 | 02/03/98 | O'Brien | |
| | A16 | 5,756,349 | 05/26/98 | Lin | |
| | A17 | 5,767,078 | 06/16/98 | Johnson et al. | |
| | A18 | 5,773,569 | 6/30/98 | Wrighton et al. | |
| | A19 | 5,830,851 | 11/03/98 | Wrighton et al. | |
| | A20 | 5,835,382 | 11/10/98 | Wilson et al. | |
| | A21 | 5,856,298 | 01/05/99 | Strickland | |
| | A22 | 5,888,772 | 03/30/99 | Okasinski et al. | |
| | A23 | 5,955,422 | 09/21/99 | Lin | |
| | A24 | 6,165,78/3 | 12/26/00 | Weiss et al. | 1 |
| | A25 | 4,658,019 | 04/14/87 | Kung et al. | |

FOREIGN PATENT DOCUMENTS

EXAMPLER NYI-39/2311v2

^{*}FXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and no onsidered. Include copy of this form with next communication to applicant.

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|---|------------------|--|
| LIGT OF DEFENDINGES CITED BY ADDITIONAL | ATTY. DOCKET NO. | APPLICATION NO. 10/520,140 (National Stage of PCT/US2002/021350) |
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| | Brines et al. | |
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|---|-----|--|----------|---|--|---|
| E | 301 | JP 5-246885 | 09/24/93 | JP-A Kokai | | · |
| E | 302 | WO 94/24160 | 10/27/94 | Brigham and Women's Hospital | y | |
| E | 303 | WO 95/05465 | 02/23/95 | Amgen, Inc. | | |
| E | 304 | WO 97/18318 | 05/22/97 | Takara Shuzo Co., Ltd. | | |
| E | 305 | WO 97/32895 | 12/12/97 | Regents of the University of California | | |
| E | 306 | WO 98/18926 | 5/07/98 | G.D. Searle & Co. | | |
| E | 307 | WO 00/35475 | 06/82/00 | Ehrenreich | | |
| E | 308 | WO 01/82952 | 11/08/01 | Action Pharma APS | * **** | |
| F | 309 | WO 01/82953 | 11/08/01 | Action Pharma APS | | |
| E | 310 | EP 555880 | 08/18/93 | Bristol-Myers quibb Company | | |
| E | 311 | WO 92/08493 | 5/29/92 | Prigham & Nomen's Hospital | | |
| E | 312 | WO 96/14081 | 5/17/96 | Bothringer Manheim gmbh | | |
| E | 313 | WO 02/10743 | 2/07/02 | Ortho McNeil Pharmaceutical, Inc. | | |
| | | | | | | |

| | | NON PATENT LITERATURE DOCUMENTS | |
|----------|--------|--|---|
| Examiner | \Box | | T |
| Initials | | (Include name of the author (in CAP/TAL LETTERS), Title, Nate, Pertinent Pages, Etc.) | T |
| | C01 | ALAFACI et al., 2000, "Effect of Recombinant Human Erythropoietin on Cerebral Ischemia Following | 1 |
| | | Experimental Subarachnoid Hemorrhage," Eur. J. Phar., 406:219-225. | |
| | C02 | ANAGNOSTOU et al., 1994 "Erythropoietin receptor mRNA expression in human endothelial cells", Proc. | 1 |
| | | Natl. Acad. Sci. USA 91:3974-3978 | ļ |
| | C03 | ANNABLE et al., 1972, The Second International Reference Preparation of Erythropoietin, Human, Urinary, | Ī |
| | | for Bioassay," Bull. O.g. mond. Sante, 47:99-112. | |
| | C04 | ASHWELL et al., 19/8, "A Protein from Mammalian Liver that Specifically Binds Galactose-Terminated | |
| | | Glycoproteins," Meth. Enzymol., 50:287-291. | |
| | C05 | BAUER, 1995, The Oxygen Sensor That Controls EPO Production: Facts and Fancies," J. Perinat. Med., 23:7- | |
| | | 12. | |
| | C06 | BENYO et 2., 1999, "Expression of erythropoietin receptor by trophoblast cells at the human placenta", Biol. | |
| | | Reproduct 60:861-870 | |
| | C07 | BERNAUDIN et al., 1999, "A potential role for erythropoietin in focal permanent cerebral ischemia in mice", J. | |
| | | Cereb Blood Flow Metab. 19:643-651 | |
| | C08 | BEDNAUDIN et al., 2000, "Neurons and astrocytes express EPO mRNA: oxygen-sensing mechanisms that | |
| | | involve the redox-state of the brain", Glia 30:271-278 | ŀ |
| | C09 | SONDY, 1995, "The relaxation of oxidative stress and hyperexcitation to neurological disease", Proc. Soc. Exp. | |
| | ا آ | Biol. Med. 208:337-345 | |

| EXAMINER |
|---------------|
| NYI-39/2311v2 |

^{*}F. AMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and ot onsidered. Include copy of this form with next communication to applicant.

| LIST OF REFERENCES CITED BY APPLICANT (Use several sheets if necessary) | ATTY. DOCKET NO. | APPLICATION NO. 10/520,140 |
|---|------------------|--|
| | 10165-037-999 | (National Stage of PCT/US20/03/021350) |
| | APPLICANT | |
| | Brines et al. | |
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| | January 3, 2005 | 647 |
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| | | NON PATENT LITERATURE DOCUMENTS | |
|----------------------|-------------|---|---|
| Examiner Initials | | (Include name of the author (in CAPITAL LETTERS), Title, Date, Pertinent Pages, Mc.) | T |
| initiais | C10 | BRIGGS et al., 1974, "Hepatic Clearance of Intact and Desialylated Erythropoletin," Am. J. Physiol., 227:1385-1388. | |
| | C11 | BRINES et al., 2000, "Erythropoietin crosses the blood-brain barrier to protect against experimental brain injury", Proc. Natl. Acad. Sci. USA 97:10526-10531 | |
| | C12 | BRUNEVAL et al., 1998, "Erythropoietin Synthesis by Tumor Cells in a Case of Meningioma Associated With Erythrocytosis," Blood, 8, 1593-1597. | |
| | C13 | CAMISCOLI et al., 1968, "Comparative Assay of Erythropoietin Standards," Annals New York Acad. Sci., 149:40-45. | |
| | C14 | CAMPANA et al., 1998, "Identification of a neurotrophic sequence in erythropoietin", Int. J. Mol. Med. 1:235-241 | |
| | C15 | CLAUS-WALKER et al., 1984, "Spinal Cord Injury and Serum Erythropoietin," Arch. Phys. Med. Rehabil., 65:370-374. | |
| | C16 | COTES, 1968, "Quantitative Estimation of Erythropotetin," Part I. Assay and Standardization of Erythropoietin, Annals New York Acad. Sci., 149:12-17. | |
| | C17 | COTES et al., 1961, "Bio-Assay of Erythropoietic in Mice Made Polycythaemic By Exposure to Air at a Reduced Pressure," Nature, 191:1065-1067. | |
| | C18 | COTES et al., 1966, "The International Reference Preparation of Erythropoietin," Bull. Org. mond. Sante, 35:751-760. | |
| | C19 | DIAZ-BRINTON et al., 1998, "Advances and challenges in the prevention and treatment of Alzheimer's disease," Pharm. Res. 15(3):386-98 | |
| | C20 | DIGICAYLIOGLU et al. 1995, "Localization of specific crythropoietin binding sites in defined areas of the mouse brain.", Proc. Natl. Acad. Sp. USA 92:3717-3720 | |
| | C21 | DIPAOLO et al., 1992, "Effects of uremia and dialysis on brain electrophysiology after recombinant erythropoietin treatment", ASAIO J. 38:M477-M480 | |
| | C22 | DONG et al., 1992, "Receptor binding of asialoerythropoietin," A Cell. Biochem. 48(3):269-76 | |
| | C23 | DORDAL et al., 1985, "The Role of Carbohydrate in Erythropoietic Action," Endocrinol., 116:2293-2299. | |
| | C24 | DUBE et al, 1988, "Gl/cosylation at Specific Sites of Erythropoietin is Essential for Biosynthesis, Secretion, and Biological Function," J. Biol. Chem., 263:17516-17521. | |
| | C25 | EHRENREICH et al., 2002, "Erythropoietin therapy for acute stroke is both safe and beneficial", Molec. Med. 8(8):495-505 | |
| | C26 | Eur. Pharmacopoeia, 1997, p. 5. | |
| | C27 | Eur. Pharmacopoeia, Suppl. 2001, pp. 777-782. | 1 |
| | C28 | FARRELL et al., 2001, "Erythropoietin crosses the blood brain barrier", Blood 98:1 8b (abstr. # 4265; 43rd Annual Meeting of the American Society of Hematology, Orlando FL, Dec. 7-11, 2001) | |
| | C29 | FEIGIN et al., 2002, "Recent advances in Huntington's disease: implications for experimental therapeutics," Cyr. Opin. Neurol. 15(4):483-9 | |
| | C30 | PUKUDA et al., 1989, "Survival of Recombinant Erythropoietin in the Circulation: The Roll of Carbohydrates," Blood, 73:84-89. | |
| | C3 y | GARTHOFF, 1995, "Safety and Efficacy Testing of Hormones and Related Products," The Report and | |

| EXAMPLER | |
|-----------------|---|
| NYI-39/2311v2 | , |

^{*}FXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and ot onsidered. Include copy of this form with next communication to applicant.

| | ATTY. DOCKET NO. | APPLICATION NO. 10/520,140 (National Stage of |
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| LIST OF REFERENCES CITED BY APPLICANT | 10165-037-999 | PCT/US20/03/021350) |
| (Use several sheets if necessary) | APPLICANT | |
| | Brines et al. | |
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| Na contract of the contract of | | A |

NON PATENT LITERATURE DOCUMENTS Examiner Initials (Include name of the author (in CAPITAL LETTERS), Title, Date, Pertinent Pages, J Т Recommendations of ECVAM Workshop 9, A.T.L.A., 23:699-711 GOLDWASSER & al., 1974, "On the Mechanism of Erythropoietin-Induced Differentiation," XIII. The Role of C32 Sialic Acid in Erythropoietin Action, J. Biol. Chem., 249:4202-4206. GOLDWASSER et al. 1975, "An Assay for Erythropoietin in Vitro at the Milliunit Level," Endo., 97:315-323. C33 GOLDWASSER et al., "Syythropoietin: Assay and Study of Its Mode of Action," Hormone Assays, pp. 109-C34 GORIO et al., 2002, "Recombinant human erythropoietin count facts secondary injury and markedly enhances C35 neurological recovery from experimental spinal cord trauma" Proc. Natl. Acad. Sci. USA 99:9450-9455 (PNAS Early Edition www.pnas.org/cgi/doi/10.1073/pnas.142287899) GRASSO et al., 2002, "Beneficial effects of systemic administration of recombinant human erythrpoietin in C36 rabbits subjected to subarachnoid hemorrhage", Proc. Natl. Acad. Sci. USA 99:5627-5631 GREGORY et al., 1999, "GATA-1 and crythropoietin cooperate to promote erythroid cell survival by regulating C37 bcl-xL expression", Blood 94:87-96 GRIMM et al., 1990, "Improvement of brain function in hemodialysis patients treated with erythropoietin". C38 Kidney Intl. 38:480-486 HAMMOND et al., 1968, "Production, Utilization and Excretion of Erythropoietin: I. Chronic Anemias. II. C39 Aplastic Crisis. III. Erythropoietic Effects of Normal Plasma," Erythropoietin, 149:516-527. HEFTI, 1997, "Pharmacology of neurotrophic factors", Annu. Rev. Pharmacol. Toxicol. 37:239-267 C40 HENGEMIHLE et al., 1996, "Chronic reatment with ruman recombinant erythropoietin increases hematocrit C41 and improves water maze performance in mice", Physiol Behav. 59:153-156 HIRAKATA et al., 1992, "CBF and oxygen metabolism in hemodialysis patients: effects of anemia correction C42 with recombinant human EPO", Am. J. Physiol. 262:F737-F 143 HORTON et al., 1991, "Von Hoppel-Lindau Disease and Erythrocytosis: Radioimmunoassay of Erythropoietin C43 in Cyst Fluid From a Brainstem Hemangioblastoma," Neurology, 41:753-754. IMAI et al., 1990, "Physic chemical and Biological Characterization of Asialoerythropoietin," Eur. J. Biochem., C44 194:457-462. JOOSS et al., 1996, "Oyclophosphamide diminishes inflammation and prolongs transgene expression following C45 delivery of adenoviral vectors to mouse liver and lung," Hum. Gene Ther 7(13):1555-66 JUNK et al., 2002 Erythropoietin administration protects retinal neurons from acute ischemia-reperfusion C46 injury", Proc. Natl. Acad. Sci. USA 99:10659-10664 (PNAS Early Edition www.pnas.org/cgi/doi/10.1073/pnas.152321399) JUUL et al. 1998, "Erythropoietin and erythropoietin receptor in the developing human central nervous C47 system", Pediatr. Res. 43:40-49 JUUL eyal., 1998, "Tissue distribution of erythropoietin and erythropoietin receptor is the developing human C48 fetus" Early Human Devel. 52:235-249 JUUL et al., 2001, "Recombinant erythropoietin (EPO) crosses the blood brain barrier (BBB) in preterm fetal C49 sheep", Soc. for Neuroscience Abstracts 27:929 (31st Annual Meeting of the Society for Neuroscience, San **B**iego, CA Nov. 10-15, 2001) KEIGHLEY, 1968, "Further Experiences with Assays, Units, and Standards of Erythropoietin, Annals New C50 York Acad. Sci., 149:18-24.

| EXAMINER. | |
|---------------|--|
| NYI-3972311v2 | |

^{*}EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and to considered. Include copy of this form with next communication to applicant.

| LIST OF REFERENCES CITED BY APPLICANT (Use several sheets if necessary) ATTY. DOCKET NO. APPLICATION NO. 10/520,140 (National Stage of PCT/US20/3/021350) APPLICANT Brines et al. FILING DATE January 3, 2005 ARY UNIT January 3, 2005 | • | | Maria de la companya | | | |
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| | | Brines et al. | | | | |
| January 3, 2003 (2047) | | | <i> </i> | | | |
| | \ | January 3, 2003 | 1/2047 | | | |

| | | NON PATENT LITERATURE DOCUMENTS | |
|-------------------------------|----------|--|----------|
| Examiner nitials | | (Include name of the author (in CAPITAL LETTERS), Title, Date, Pertinent Pages, Itc.) | T |
| IIIIIais | 051 | KOHAMA et al., 2000, "Large Uterine Myoma with Erythropoietin Messenger RNA and Erythrocytosis," | 1 1 |
| | C51 | Obstetrics and Genecology, 96:826-828. | 1 |
| · · · · · · · · · | C52 | KONISHI et al., 1923, "Trophic effect of erythropoietin and other hematogoietic factors on central cholinergic | 1 |
| | C32 | neurons in vitro and by vivo", Brain Res. 609:29-35 | |
| | CE2 | KOPF et al., 1994, "Memory improving actions of glucose: involvement of a central cholinergic muscarinic | \vdash |
| | C53 | mechanism.", Behav. Nedral Biol. 62:237-243 | |
| | CEA | LATINI et al., 1998, "Comparative efficacy of a DA2/α2 agonist and a β blocker in reducing adrenergic drive | ╁ |
| | C54 | and cardiac fibrosis in an experimental model of left ventricular dysfunction after coronary artery occlusion", J. | |
| | | Cardiovasc. Pharmacol. 31:601 608 | |
| | C55 | LI et al., 1996, "Erythropoietin receptors are expressed in the central nervous system of mid-trimester human | ╆ |
| | CSS | fetuses", Pediatr. Res. 40:376-380 | |
| | C56 | LI et al., 1998, "A single pre training alucose injection induces memory facilitation in rodents performing | ╁ |
| | C36 | various tasks: contribution of acidic fibroblast growth factor", Neurosci. 85:785-794 | - |
| | C57 | LIPINSKI et al., 1995, "Nerve growth factor facilitates conditioned taste aversion learning in normal rats", Brain | ╁ |
| | 1037 | Res. 692:143-153 | |
| | C58 | LIU et al., 1996, "Transgenic mice containing the human erythropoietin receptor gene exhibit correct | + |
| | C38 | hematopoietic and neural expression", Proc. Assoc. Am. Physicians 108:449-454 | |
| | C59 | LIU et al., 1997, "Regulated human erythropoietin receptor expression in mouse brain", J. Biol. Chem. | + |
| | 1039 | 272:32395-32400 | |
| | C60 | LIU et al., 1994, "Tissue specific expression of human erythropoietin receptor in transgenic mice", Devel. Biol. | † |
| | 1000 | 166:159-169 | |
| | C61 | LOWY et al., 1960, "Inactivation of Erythropoietin by Neuraminidase and by Mild Substitution Reactions," | ╁╴ |
| | 1001 | Nature, 185:102-103. | |
| | C62 | MARRERO et al., 1998, "Erytt ropoietin receptor-operated C2+ channels: activation by phospholipase C-γ1", | |
| | 002 | Kidney Intl. 53:1259-1268 | |
| | C63 | MARSH et al., 1991, "rHugePO treatment improves brain and cognitive function of anemic dialysis patients", | |
| | | Kidney Intl. 39:155-163 | |
| | C64 | MARTI et al., 1997, "Detection of erythropoietin in human liquor: intrinsic erythropoietin production in the | |
| | | brain", Kidney Intl. 5/:416-418 | |
| | C65 | MARTI et al., 1996, "Erythropoietin gene expression in human, monkey and murine brain", Eur. J. Neurosci. | 1 |
| | 555 | 8:666-676 | |
| | C66 | MASUDA et al., 1997, "Insulin like growth factors and insulin stimulate erythropoietin production in primary | |
| | | cultured astrocytes", Brain Res. 746:63-70 | |
| | C67 | MASUDA et al., 1994, "A novel site of erythropoietin production. Oxygen dependent production in cultured rat | Π |
| | | astrocyte*, J. Biol. Chem. 269:19488-19493 | |
| | C68 | MASUDA et al., 1993, "Functional erythropoietin receptor of the cells with neural characteristics. Comparison | Τ |
| | | with receptor properties of erythroid cells", J. Biol. Chem. 268:11208-11216 | |
| | C69 | MATSUYAMA et al., 2000, "Erythrocytosis Caused by an Erythropoietin-Producing Hepatocellular | 1 |
| | | Garcinoma," J. Surg. Oncology, 75:197-202. | |
| | C70 | MIONI et al., 1992, "Evidence for specific binding and stimulatory effects of recombinant human erythropoietin | \top |
| | <i>M</i> | on isolated adult rat Leydig cells", Acta Endocrinologica 127:459-465 | 1 |

| EXAMINER | |
|------------------------|--|
| NYI-39 7 2311v2 | |

^{*}EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

10520140 - GAU: 16 Express Mail No.: DRAF Sheet 6 of 7 of List of References

| | ATTY. DOCKET NO. | APPLICATION NO. 10/520,140 |
|---|------------------|---------------------------------------|
| LIST OF REFERENCES CITED BY APPLICANT (Use several sheets if necessary) | 10165-037-999 | (National Stage of PCT/US2003/021350) |
| | APPLICANT | 1.01/03/03/02/330) |
| | Brines et al. | |
| | FILING DATE | ATUNIT |
| | January 3, 2005 | 1647 |

| | | NON PATENT LITERATURE DOCUMENTS | |
|----------------------|-----|--|---|
| Examiner Initials | | (Include name of the author (in CAPITAL LETTERS), Title, Date, Pertinent Pages Etc.) | Т |
| | C71 | MIYAKE et al., 1977, "Purification of Human Erythropoietin," J. Biol. Chept., 252:5558-5564. | 1 |
| | C72 | MORELL et al., 1 68, "Physical and Chemical Studies on Ceruloplasmin," Metabolic Studies on Sialic Acid- Free Ceruloplasmin Vivo, J. Biol. Chem., 243:155-159. | |
| | C73 | MORISHITA et al., 1997, "Erythropoietin receptor is expressed in rat hippocampal and cerebral cortical neurons, and erythropoietin prevents in vitro glutamate induced neuronal death", Neurosci. 76:105-116 | |
| | C74 | MOSS et al., 1996, "Oxygen administration enhances memory formation in healthy young adults", Psychopharmacol. 124:255-260 | |
| | C75 | NAKAMURA et al., 1998, "Elevated levels of erythropoieting neerebrospinal fluid of depressed patients", Am. J. Med. Sci. 315:199-201 | |
| | C76 | NISSENSON et al., 1991, "Recombinant human erythropoietin and renal anemia: molecular biology, clinical efficacy and nervous system effects", Ann. Int. Med. 114:402-416 | |
| | C77 | NISSENSON, 1989, "Recombinant human erythropoletin: impact on brain and cognitive function, exercise tolerance, sexual potency and quality of Ike", Sem. Nephrol. 9(suppl. 2):25-31 | |
| | C78 | OGDEN, 1989, "Monitoring consideration in recombinant human erythropoietin therapy", Sem. Nephrol. 9(suppl. 2):12-15 | |
| | C79 | OKADA et al., 1996, "Erythropoietin stimulates proliferation of rat-cultured gastric mucosal cells", Digestion 57:328-332 | |
| | C80 | PARDRIDGE, 1997, "Drug delivery to the brain", A Cerebral Blood Flow Metab. 17:713-731 | |
| | C81 | PARDRIDGE et al., 1991, "Selective transport of an anti-transferrin receptor antibody through the blood-brain barrier in vivo", J. Pharmacol. Exp. Ther. 27:66-70 | |
| | C82 | PLAPP et al., 1971, "Activity of bovine pancreatic deoxyrhonuclease A with modified amino groups," J. Biol. Chem. 246(4):939-45 | |
| | C83 | PODUSLO et al., 1994, "Macomolecular premeability across the blood-nerve and blood-brain barriers", Proc. Natl. Acad. Sci. USA 91:5795-5709 | |
| | C84 | PRENDERGAST et al., 1997, "Nitric oxide synthase inhibition impairs spatial navigation learning and induces conditioned taste aversion", Pharmacol. Biochem. Behav. 57:347-352 | |
| | C85 | ROBINSON et al., 1975, "Tetanus toxin. The effect of chemical modifications on toxicity, immunogenicity, and conformation," J. Bjøl. Chem. 250(18):7435-42 | |
| | C86 | ROSE et al., 1998 'Receptor-mediated angiotensin II transcytosis by brain microvessel endothelial cells", Peptides 19:1023-1030 | |
| | C87 | SADAMATO et al., 1998, "Erythropoietin prevents place navigation disability and cortical infarction in rats with permanent occlusion of the middle cerebral artery", Biochem. Biophys. Res. Comm. 253:26-32 | |
| | C88 | SAKANAKA et al., 1998, "In vivo evidence that erythropoietin protects neurons from ischemic damage", Proc. Natl. Açad. Sci. USA 95:4635-4640 | |
| | C89 | SATAKE et al. 1990, "Chemical modification of erythropoietin: an increase in in vitro ctivity by guardination," Biochim. Biophys. Acta. 1038(1):125-9 | |
| | C90 | SAWYER et al., 1989, "Receptors for erythropoietin in mouse and human erythroid cells and placenta", Blood 74:103-109 | |
| | C91 | SHIRAMIZU et al., 1994, "Constitutive Secretion of Erythropoietin by Human Renal Adenocal inoma Cells in Vivo and in Vitro," Exp. Cell Res., 215:249-256. | T |

| EXAMI | Ł | ER |
|-----------|---|-----|
| NYI-39/23 | ı | lv2 |

^{*}FXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

10520140 - GAU: 164 Express Mail No.: DRAFT Sheet 7 of 7 of List of Reference

| 1 | | A . |
|---------------------------------------|---------------------------------|--|
| LIST OF REFERENCES CITED BY APPLICANT | ATTY. DOCKET NO. 10165-037-999 | APPLICATION NO. 10/520,140 (National Stage of PCT/US2003/021350) |
| (Use several sheets if necessary) | APPLICANT | |
| | Brines et al. | |
| | Brines et al. | |
| | FILING DATE | ARTUNIT |
| 1 | January 3, 2005 | / 647 |
| | | |

NON PATENT LITERATURE DOCUMENTS Examiner Т (Include name of the author (in CAPITAL LETTERS), Title, Date, Pertinent Pages, Initials SHORE et al., 1968, "Quantitative Estimation of Erythropoietin," Annals New York Acad. Sci., 149:46-48. C92 SILVA et al., 1998, "Erythropoietin can induce the expression of bcl-xL through Stat5 in erythropoietin-C93 dependent progenitor cell lines", J. Biol. Chem. 274:22165-22169 SIRÉN et al., 2001, "Exythropoietin prevents neuronal apoptosis after gerebral ischemia and metabolic stress", C94 Proc. Natl. Acad. Sci. USA 98:4044-4049 SPIVAK et al., 1989, "The In Vivo Metabolism of Recombinant Human Erythropoietin in the Rat," Blood, C95 73:90-99 STARK et al., 1960, "Reactions of the Cyanate Present in Aqueous Urea With Amino Acids and Proteins," J. C96 Biol. Chem. 235(11): 3177-318 STEECE-COLLIER et al., 2002, "Etiology of Parkinson's isease: Genetics and environment revisited," Proc. C97 Natl. Acad. Sci. U. S. A. 99(22):139 2-4 STORRING et al., 1998, "Epoietin Alia and Beta Differ In Erythropoietin Isoform Compositions and Biological C98 Properties," British J. Haematology, 100 79-89. STORRING et al., 1992, "The International Standard for Recombinant DNA-Derived Erythropoietin: C99 Collaborative Study of Four Recombinant DNA derived Erythropoietins and Two Highly Purified Human Urinary Erythropoietins," J. Endocrinol., 134 59-484. SUZUKI et al., 2001, "Erythropoietin Synthesis by Tumour Tissues in a Patient With Uterine Myoma and C100 ERythrocytosis," British J. Haematology, 13:49-3 TABIRA et al., 1995, "Neurotrophic effect of hemail poietic cytokines on cholinergic and other neurons in C101 vitro", Int. J. Devl. Neurosci. 13:241-24 WEILAND et al., "In vivo Activity Asialo-Erythropoletin in Combination with Asialo-Glycoproteins," 1982, C102 Blut, 44:173-175. WESTENFELDER et al., 1999, Human, rat and mouse kidney cells express functional erythropoietin C103 receptors", Kidney Intl. 55:808-820 WILLIAMS et al., 1994, "Haman crythropojetin receptor", Ann. NY Acad. Sci. 718:232-244 C104 WOLCOTT et al., 1989, Recombinant human erythropoietin treatment may improve quality of life and C105 cognitive function in chronic hemodialysis patients", Am. J. Kidney Dis. 14:478-485 WU et al., 1999, "Ne roprotection with noninvasive neurotrophin delivery to the brain", PNAS 96:254-259 C106 YAMAJI et al., 196, "Brain capillary endothelial cells express two forms of erythropoietin receptor mRNA", C107 Eur. J. Biochem 239:494-500 YANG et al., 2002, "Effects of ammonia and glucosamine on the heterogeneit of crythropoietin glycoforms," C108 Biotechnol. Frog. 18(1):129-38

| EXAMINER |
|----------------|
| NYI-397/2311v2 |

^{*}EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.